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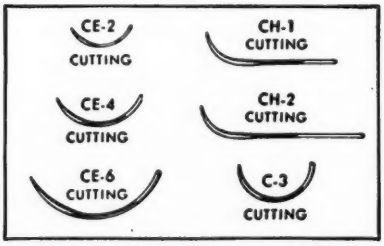

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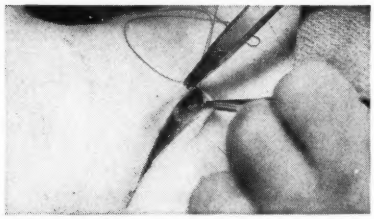

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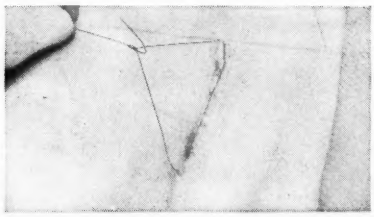

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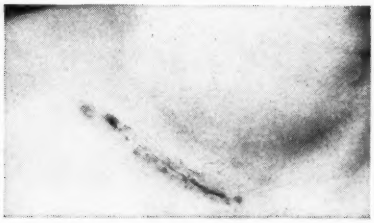

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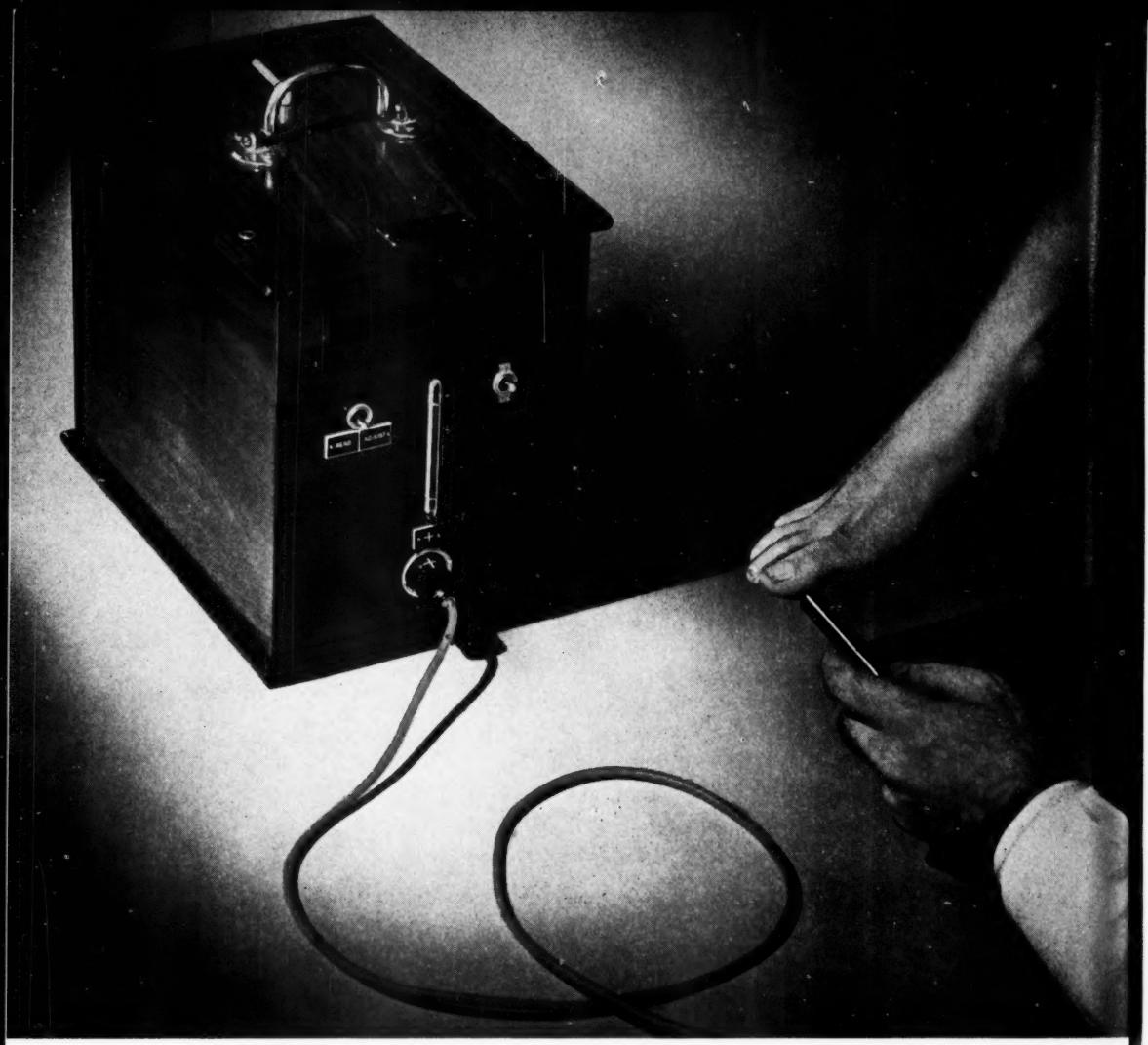

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SURGERY
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THERMAL BURNS FROM THE ATOMIC BOMB

HERMAN E. PEARSE, M.D., F.A.C.S., and HARRY D. KINGSLEY, M.D., Rochester, New York

THE primary burn from an atomic bomb explosion is caused by a brief exposure to high intensity radiant thermal energy, whereas the usual burn seen in civil life is from contact with lower temperatures. How this difference affects the local lesion, its systemic effect, clinical course, and mortality are not known.

Tsuzuki stated that 90 per cent of the Japanese who sought aid in the first week after the atomic bombing did so because of thermal burns. In Hiroshima alone, there were approximately 70,000 cases of burns of which about 40,000 were serious. This created an enormous problem (Fig. 1) of clinical management which could not be satisfactorily handled. There is not yet a practical plan for the immediate mass treatment of so many burn casualties. The first requisite of rational therapy is to understand the lesion to be treated. Hence, the first step toward the solution of the problem of the mass management of flash burns from the atomic bomb was knowledge of the characteristics of this injury.

In spite of the thousands of flash burns at Hiroshima and Nagasaki, there was not a single immediate biopsy available to illustrate the histologic changes produced in skin. This was understandable in view of the confusion and difficulties created, but it did not give a picture of the lesion in man. Many histologic sections from Japanese casualties were reviewed, but all were obtained late after infection or repair had set in. Likewise, at the Bikini tests, when emphasis was focused on the effect of ionizing irradiation on the animals exposed, no immediate skin biopsies of thermal burns could be found. Thus, the investigator who attempted to reproduce flash burns from the atomic bomb in the laboratory had no way to check the accuracy of his methods. He did not know the gross or histologic appearance of the burns, their energy or spectral relationships, the time of their production, or the method of their healing. These data could only be obtained by experiments which actually exposed the skin of animals to the thermal energy from atomic bomb explosions.

In the laboratory, skin biopsies of the flash burns in experimental animals showed a direct relationship between the depth of injury and amount of energy applied (1, 4). In order to confirm this in the field it was necessary to evaluate the relationship of the intensity of the thermal energy from an atomic bomb to the severity and depth of the burn. This would define the burn as a function of energy.

Time dependence of burn production from the atomic bomb explosion was a matter of dispute which was argued on theoretic grounds. There were no data from observations of burning as a function of time after the explosion. In the manual, "The Effects of Atomic Weapons" Figure 6.6 showed an initial high intensity which dropped to a minimum of approximately 2,000 degrees K. in about 15 milliseconds. A short null was

From the Department of Surgery and the Atomic Energy Project of the University of Rochester, School of Medicine and Dentistry, Rochester, New York.

TABLE 1.—GRADING OF LESIONS

Grade	Surface appearance	Descriptive term	Cal./cm². in 0.3 sec.
1+	Erythema	Red burn	2.3
2+	Patchy coagulation	Spotted white burn	4.5
3+	Uniform coagulation	White burn	7.5
4+	Steam bleb	Blebbed white burn	10.0
5+	Carbonization	Charred burn	19.0

followed by a rise to a second maximum of about 7,000 degrees K. in 0.3 second after which the temperature fell. Nearly all of the thermal radiation was emitted in 3 seconds.

The initial flash attained a very high temperature but lasted only 15 milliseconds. Because of the short duration, only 1 per cent of the total thermal energy was delivered in this period. Yet it was thought by some that, due to the high temperature and high ultraviolet content, flash burns occurred in this stage. This was tested.

As previously noted, the second maximum occurred in about 0.3 second and the majority of the radiation from the ball of fire was delivered in 3 seconds. It was necessary to determine when flash burns occurred in this period at different distances from the explosion to show whether or not evasive action by exposed personnel could modify the burns.

The influence of thermal energy of various regions of the spectrum in the production of flash burns from the atomic bomb should be known. The depth of penetration varied directly with wave length, ultraviolet being the least and infrared the most penetrating. In addition to pure thermal injury, ultraviolet had a photochemical effect which reached a maximum at 2,970 angstroms. Wave lengths below 1,900 angstroms were absorbed by ozone. Since atmospheric attenuation was greatest for the shorter wave lengths, it was probable that they could be disregarded at the distant perimeters.

The thermal energy released by the bomb explosion might be modified by nitrogen dioxide, ozone, atmospheric opacity to short wave lengths, scattering, absorption, and other attenuating factors. This might make extrapolation difficult, so it was desirable to measure the energy incident on the experimental animals.

It was well known from observations made upon the Japanese that the color, thickness, and composition of clothing modified the burns. Some garments protected the skin from injury when burns of the exposed skin occurred. Limited observations have been made on the protective effect of some fabrics against burns from thermal radiation of bomb. These have been amplified in the laboratory (3, 5).

METHODS

Animals. Most of the work in this laboratory has been done on young Chester White pigs because their skin is so similar to that of man. Ninety-one Chester White pigs have been exposed during experiments at bomb tests. At one test 8 Danish Landrace pigs of mixed brown and black color and 15 adult fox hounds were used alongside the white pigs to observe the effect of color and species differences. Animals were either born and reared at the test site or were acclimated there for a sufficient time to assure good health. They were always under the care of a competent veterinarian, were well fed, and were kept in clean, comfortable open runs having a lean-to shelter at one end.

Prior to a test the area of skin to be exposed was closely clipped using power shears having a No. 40 head. Shaving or depilatories were not used for they had been found to cause skin irritation. The animals were then placed in well ventilated containers, transported to the exposure stations, anesthetized, and positioned behind individual exposure plates in structures constructed to withstand blast.

Anesthesia. Operational requirements made it necessary to place the animals in the stations some hours or even a day before they were exposed. Hence, a long-acting anesthetic without explosive hazards was necessary to assure anesthesia at the time of burning. We found that dial in urea-urethane injected intraperitoneally was satisfactory in doses of 70 to 75 milligrams of dial per kilogram body weight for pigs, and 60 milligrams per kilogram for dogs (2). The best results were obtained after fasting the animals for 24 hours prior to induction of anesthesia. The fasting weight was used for calculation of dosage.

Location of stations. The thermal energy from an atomic bomb explosion is attenuated by passage through the atmosphere. Thus,

burn severity will be a function of the distance from the bomb. In order to examine the effect of different levels of thermal energy on animal skin, stations were located to give exposures of 1.1, 2.2, 3.8, 5.3, 9, 10, 12, 15, 20, 25, 28, 34, 36, and 43 calories per square centimeter. This was designed to give a range of all grades of severity from no burn to a char which provided a comparison with burns created in the laboratory.

The laboratory observations (4, 6) of over 1500 burns done under variable conditions of time and intensity of applied thermal energy from a carbon arc searchlight had established five criteria of severity of surface damage which permitted grading of lesions. The laboratory grading system is shown in Table I.

Changing the time of exposure altered the energy required to produce any given grade. By means of these standards it was possible to evaluate the burns created by the atomic bomb in terms of the thermal energy required for production of equivalent lesions in the laboratory. This level of energy could then be compared to that actually measured in the field.

Shelters. Stations were designed to give adequate protection against calculated overpressure from the blast and to minimize the effects of ionizing irradiation on the contained animals. In the side of the station facing the bomb burst were ports behind which were bolted heavy aluminum plates with apertures through which thermal radiation passed. In some stations two animal containers, one above the other, were bolted to the back of the port in such a fashion that the flanks of the exposed animals were in contact with the apertures. The stations were ventilated with battery-operated blower and duct systems. Temperature and ventilation were regulated according to the needs of the animals as determined by environmental studies made in the area prior to building the shelters.

Aperture plates. The exposure aperture plates were of three types, each constructed of ¾ inch aluminum alloy, 6 by 12 inches in size. All openings in the plates were covered by fused quartz windows to eliminate sand blasting of the skin. Each of the three plates had at least one aperture which was not modified by a shutter, filter or fabric, so that each animal received the total integrated energy on this area of skin as a control.

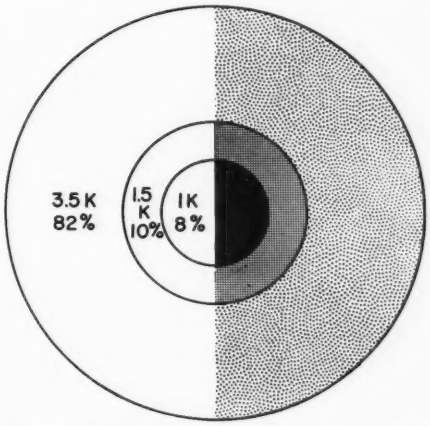


Fig. 1. A schematic representation which assumes a uniform density of population exposed to a "nominal" 20 kiloton atomic bomb. The zone having a 1 kilometer radius, shown in black, where total destruction occurs contains 8 per cent of the population. The crosshatched zone between 1 and 1.5 kilometers contains 10 per cent, many of whom will have sublethal ionizing irradiation sickness combined with burns or wounds. The area between 1.5 and 3.5 kilometers has 82 per cent of the population at risk who will be exposed to thermal burns or wounds, but not to serious ionizing irradiation. Here definitive surgical care will give high rewards.

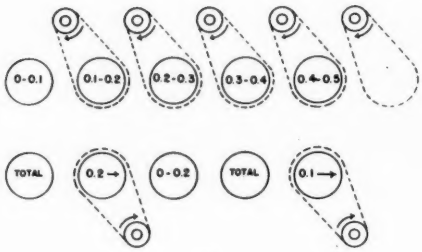
The smallest hole in any aperture plate was 1.9 centimeters (0.75 in.) in diameter. This gave an adequate opening for good burns but it was believed to be close to the minimum consistent with biologic validity because of edge effects. The openings ranged from this size up to 3 by 4½ inches. Burns through small and large apertures were compared side by side to observe differences in severity of burns between small and large area exposures.

All of the timing shutters were activated by photoelectric relays which were initiated by the flash of the bomb. Equipment was wired through a central control panel. Power was supplied either from storage batteries or from power lines depending upon the location of the stations.

The types of aperture plates were as follows:

1. Shutters for time resolution.

a. Fast shutter.—This plate had 3 round apertures. One was 2.2 inches in diameter



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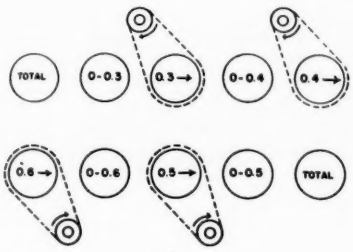


b

Fig. 2. A diagram of the pair of shutters used for multiple time resolution of the burn after detonation of an atomic bomb. a, In shutter No. 1, top row, the first port is open at bomb zero. As the diaphragm swings to close, at 0.1 second, it opens the next port for the interval 0.1 to 0.2 second and so on. The second row has two open ports giving total burns, also one giving a burn after 0.1 second and ports exposing for the first 0.2 second and after 0.2 second. b, In shutter No. 2 the ports follow this sequence by permitting exposure before and after periods of 0.3, 0.4, 0.5, and 0.6 second.

providing the unmodified exposure. The two remaining apertures were 1.125 inches in diameter. At the time of the flash from the explosion, one of these ports was open and the other was covered by a spring-loaded aluminum shutter. The shutter was timed to cover the open port and open the closed one at 20 to 25 milliseconds, during the null between the two maxima. It was planned to give an evaluation of the burn produced by the initial flash in comparison to that from the ball of fire.

b. Slow strip shutter.—This plate contained one rectangular aperture, 2 by 8 inches in size, placed horizontally. A quartz window covered the entire area. Behind the window was a thin sliding shutter which had an opening 2 by 5 inches. Travel of the slide was initiated by a photocell signal. Transport time for the shutter was 2 seconds. By this method, 3 inches at one end of the rectangular opening in the plate was closing and 3 inches at the other end was opening during the 2 seconds following the initiation of the explosion. The central 2 inches was open throughout the exposure. This provided for assessment of the severity of the burn in the first 2 seconds after explosion.

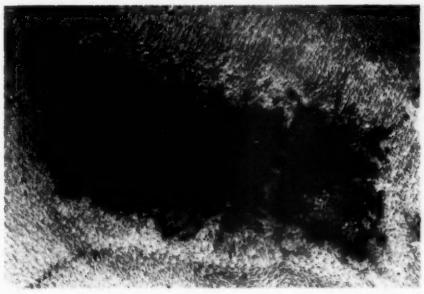
c. Multiple time shutter.—From experience gained with the two shutters described, it was believed that a more accurate time resolution was necessary so a third type was designed (Fig. 2) and used at subsequent bomb explosions. It was planned to obtain information on the time in which the thermal burns were sustained after detonation of a bomb as follows: (1) the severity of burns produced in the first 5 consecutive 0.1 second periods; (2) the amount of burning which was produced at 6 periods having 0.1 second increments from 0 to 0.1 through 0 to 0.6 second; (3) the severity of 6 burns created by decreasing the exposure progressively, cutting off successive increments of 0.1 second from the beginning of the pulse. This gave exposures covering the periods of 0.1 second to the end of the pulse through 0.6 second to the end of the pulse; (4) the severity of the total, unmodified burn to serve as a control at each distance.

Each shutter plate had two rows of five 1.5 inch circular apertures in an overall area of 4 by 10 inches. Each aperture was covered with fused quartz to prevent sand-blasting of the animal's skin during the shock wave.

The operation of the solenoid activated shutter plates was initiated by the flash of the bomb on photoelectric relays.

2. Filter plate.

This plate had four round apertures. One of these was 2.25 inches in diameter and had only a clear quartz window covering it. The other three openings were 1.375 inches in diameter and were covered by optical filters. The filters used for infrared transmission were Corning No. 2404, Sharp cut-off red glass which cut in at 6,500 angstroms. For the visible region, Pittsburgh heat-absorbing glass was found to be the most satisfactory because it had a high transmission, between 4,000 and 8,000 angstroms, but it passed some infrared



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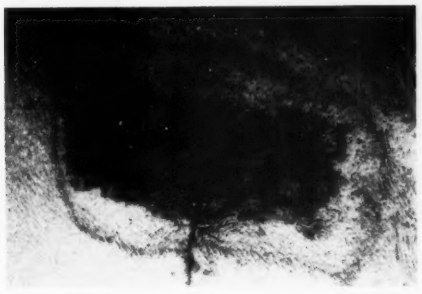

b

Fig. 3. a, The appearance of a severe 5+ carbonized burn in Chester White pig No. 265, 13 hours after exposure to 34 calories per square centimeter. b, The same lesion 122 hours after burning. Note the zone of white coagulation surrounded by a ring of erythema outside the carbonized burn. A biopsy wound is in the lower margin.

beyond this main spectral region. For the ultraviolet filter, it was found necessary to use a combination of 60 per cent aqueous solution of nickel sulfate and the Corning No. 9863 glass for two reasons: first, the No. 9863 glass tended to crack with moderate temperature changes, and second, both the No. 9863 glass and the nickel sulfate solution had minor transmission bands in the visible which the combination eliminated. It had 60 per cent transmission at 3,000 angstroms with a range of 2,500 to 3,300 angstroms.

3. Fabric plate.

This plate was the same as that described for the use of filters with the exception that fabrics to be tested replaced the optical filters used. Quartz glass covered the openings in the plate behind which were placed herringbone twill cotton, serge and sateen, with or without undershirt material. The skin of the animal's flank was placed in contact with the fabrics. In this way an attempt was made to assess the protective effect of these fabrics in preventing skin burns.

Instrumentation. Two types of measurement of the thermal energy causing the burns have been used. At some tests a radiation calorimeter which measured total integrated energy was placed in each station so that the instrument measured the energy passing through the unmodified ports and through each of the optical filters at every location. This calorimeter had the disadvantage of giving total integrated energy without time resolution. At subsequent tests time-intensity measurements were made by others at points adjacent to the exposed animals so that a time resolution was obtained to compare the severity of the burn and the incident energy.

Evaluation of burns. As soon as possible after exposure, animals were retrieved from the stations and returned to the field laboratory. Additional anesthesia was administered if necessary. Careful gross evaluation of the lesions was made, identification checked, and the burns photographed in color. Biopsies of skin lesions were then performed. Biopsy material was identified, fixed, and embedded in paraffin blocks using Auto-Technicon equipment. The tissues were then returned to the laboratory in Rochester, New York, for sectioning, mounting, and microscopic study. Following biopsy, the animals were returned

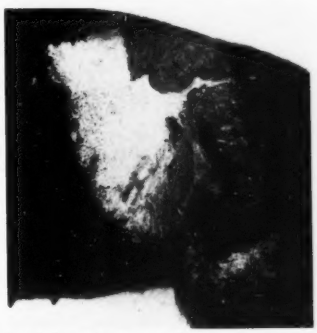

Fig. 4. A 5+ burn from 34 calories per square centimeter in Danish Landrace pig No. 268 at 360 hours (15 days) after injury, showing shedding eschar with underlying healed depigmented epithelium. The animal later died of irradiation sickness.

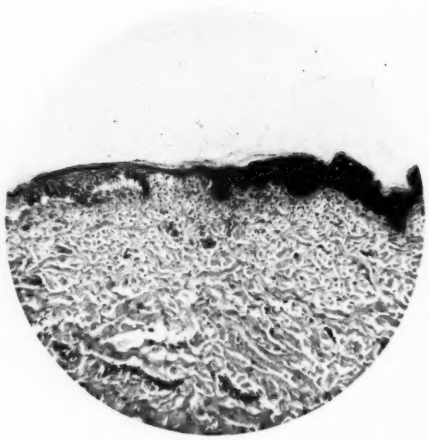

Fig. 5. The transepidermal injury in Chester White pig No. 224, 15 hours after exposure to 6.9 calories per square centimeter. In the center is seen the sharp demarcation between injured epidermis to the left and uninjured to the right.

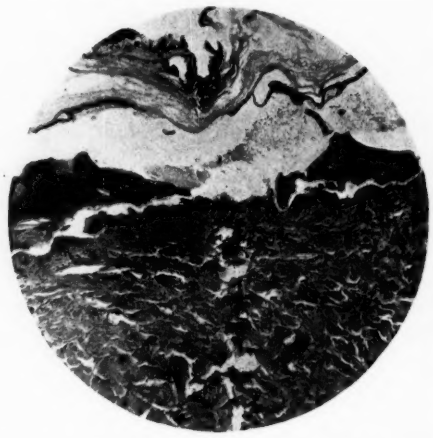

Fig. 6. Section (×33.6) of Chester White pig No. 270, 13 hours after exposure to 34 calories per square centimeter. There is coagulation and destruction of the epidermis but no obvious demarcation of the depth of the burn in the dermis at this time.

to the runs, allowed to recover from anesthesia, and observed daily for healing of the burns. Repeated biopsies and photographs were done as indicated during the healing of the lesions. A clinical record of daily observations was made on each animal.

RESULTS

Pathology and course of burns. The lesions produced in the white pigs in the field were similar to those seen in the laboratory from application of high intensity radiant energy from the carbon arc or burning magnesium.

Fig. 7. Section (×33.6) of Danish Landrace pig No. 269 taken 74 hours after exposure to 34 calories per square centimeter. The line of demarcation in depth is indicated both by the basophilic staining of the burned dermis and the inflammatory reaction between living and dead tissue.

Fig. 8. Section (×33.6) of Chester White pig No. 270, 122 hours after exposure to 34 calories per square centimeter. A wedge-shaped layer of epithelium has grown out of the hair follicle in the lower left corner and is proliferating under the thick eschar.

The dry, coagulated surface without much edema, cyanosis, or weeping of serum was the same. In the severe burns (Fig. 3) the character of the central carbonization and peripheral white ring surrounded by hyperemia was exactly like that produced by the carbon arc. In all grades of severity from a mild hyperemia to a char the burns produced by the bomb explosion duplicated those seen in the laboratory. The clinical course and healing by sequestration of the eschar (Fig. 4) were similar. They were unlike low temperature, contact burns which were variable in depth and edematous in their early stages.

Histologically these burns also resembled those produced in the laboratory by radiant energy for they had the same striking demarcation laterally (Fig. 5) and in depth that has been described as characteristic of the flash burn (1). The injury penetrated uniformly to a horizontal line where there was abrupt demarcation between living and dead tissue.

The healing of bomb burns of all grades of severity was like that of similar burns created from laboratory sources. In both, the coagulated surface formed a tough eschar which appeared to seal the damaged area. The epithelium grew from the intact hair follicles and proliferated under the eschar to cover the injured surface just as it did in the experiments reported on burns from magnesium. The eschar then sequestrated leaving an epithelialized surface.

Fig. 9. Section (×33.6) of Danish Landrace pig No. 269, 228 hours after exposure to 34 calories per square centimeter. The new epidermis has completely regenerated beneath the eschar which has separated in this location, but is loosely attached elsewhere. At this stage, the eschar may be easily pulled off exposing a healed surface beneath.

Figure 6 shows the microscopic appearance of a 5+ burn in a Chester White pig 13 hours after exposure to 34 calories per square

a

b

Fig. 10. A comparison of depth of injury as indicated by the thickness of the eschar at 124 hours in (a) white pig No. 202 and (b) in black pig No. 207 both with the same exposure to 10 calories per square centimeter (×44). Restoration of the epidermis is also more advanced in the white pig.

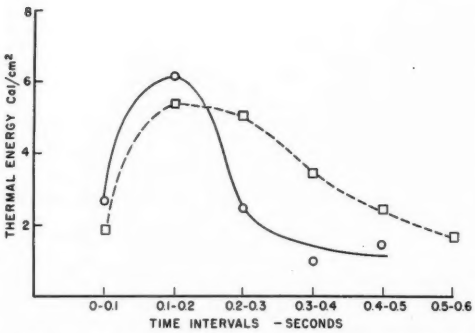

Fig. 11. The atomic bomb burn has been evaluated in terms of the number of calories per square centimeter required to cause an equivalent lesion in the laboratory. The burns shown in solid line were most severe in the period between 0.1 and 0.2 second after bomb detonation. The measured thermal energy, shown in the dotted line, correlates well for the first two 0.1 second intervals but was consistently higher after this time.

centimeter. The epidermis was coagulated on either side and completely destroyed in the center. Nuclear pyknosis and change in staining were seen in the upper layer of the dermis, but the exact depth of the burn was not apparent at this time. In all sections taken soon after burning, the level of demarcation in depth was not obvious. Demarcation is well seen in Figure 7 which is a section of pig skin 74 hours after exposure. The injured dermis then had a basophilic staining reaction, the blue color of which contrasted sharply with the red eosinophilic staining of the viable tissue. There was an inflammatory zone of leucocytic infiltration at the base of the dead tissue which separated it from the living dermis. Healing by proliferation of epithelium from the uninjured hair follicles was beginning.

The method of repair is seen in Figure 8 which shows a section of pig skin taken 122 hours (5 days) after exposure. In this illustration, the epithelium is shown growing from the uppermost viable epidermis of the hair follicle and proliferating in a sheet beneath the eschar formed by the devitalized tissue. This proliferative response of the epithelium proceeded from all viable hair follicles with eventual meeting and blending of the individual sheets to form a new epidermis. Seen in section, this process began as a heaping up of epidermis at either side of the hair follicle followed by peripheral extension of a thin projection of epithelium often only one or two cells thick. As this process proceeded away from the parent follicle, proximally it became thicker and took on the appearance of epidermis with new papillae while the leading edge remained thin. Figure 9 shows the healing obtained in a pig at 228 hours (9½ days) after exposure to 34 calories per square centimeter. It is seen that the burned tissue was separated off the surface of the epidermis and covered it only as an eschar attached by hairs and small areas of delayed healing.

Species differences in response to thermal energy. Grossly, dogs sustained more severe burns than did the white pigs exposed at the same stations. In 4+ and 3+ burns the skin of the dogs showed greater contracture and depression of the surface in the early stages. In 48 to 72 hours there was surrounding edema and the central burned area cracked and began to ooze serum and pus. Sloughing of the area occurred early leaving a dirty granulating surface which healed by contracture and marginal epithelialization. The less severe burns in the dogs were not striking in the early phases although some edema was present. In 24 to 48 hours there was increased swelling and serum began to weep from the wound. Some of these lesions sloughed. The dark colored pigs received more severe burns with deeper penetration (Fig. 10) of injury than did white pigs exposed at the same stations. The healing time was longer in the dogs and black pigs than in the white pigs. With exposure to 6.9 calories per square centimeter the average healing time of the burns on white pigs was 8 days; of those on black pigs, 16 days; of those on dogs, 19 days.

Burns produced behind filters. Twenty-four animals were exposed behind filter aperture plates which transmitted the unmodified radiant energy and that in the ultraviolet, visible, and near infrared portions of the spectrum respectively.

Through the port which admitted only the ultraviolet light, there were no burns produced in any of the animals at any station.

These animals were observed carefully to determine if any delayed reaction occurred from the photochemical effects of ultraviolet light, but none was seen.

The burns produced behind the filter passing visible light were of the same degree of severity as those produced behind the infrared filters in 7 animals. In 4 animals slightly more severe burns were sustained behind the visible than behind the infrared filters.

The burns through the unmodified openings in the filter plates were always more severe than those through limiting filters at the same station. The clinical behavior and healing of the lesions produced behind visible and infrared filters were identical to that of unmodified burns of similar severity.

Burns produced as a function of time. There were 19 pigs and 5 dogs exposed behind the fast shutter which separated the burn caused by initial flash and the fire ball. These fast shutters were set to shift at 20 to 25 milliseconds, and in no instance was a burn sustained behind the aperture which was open during this period. Burns sustained through the ports which were open after 20 to 25 milliseconds were equal in severity to those through the unmodified ports.

There were 19 pigs and 5 dogs placed behind the slow strip shutter. Each shutter was arranged so that the 5 inch opening shifted 3 inches in 2 seconds in a cephalad direction. The burns produced appeared uniform over the caudad 5 inch length which was that part exposed initially behind the opening. Some showed an additional 3/8 inch to 1/2 inch of a less severe burn at the cephalad end of this strip. Since this distance was traversed in 1/3 second the burn was produced in this time.

There were 24 white pigs exposed behind the multiple time shutters. It was found that: (1) The skin burns produced in the period between 0.1 and 0.2 second after bomb detonation were the most severe of any created by a 0.1 second interval of the thermal pulse (Fig. 11). (2) By increasing increments of exposure, the major severity of thermal burns was attained within the first 0.3 second and the maximum severity within the first 0.5 second after bomb zero. (3) No burns were produced if the skin was shielded from the first 0.6 second of the thermal pulse. Yet the calculated amount of thermal energy after this period was 30 per cent of the measured incident energy. (4) There was fair relationship during the first 0.2 second between the measured thermal energy and that determined by evaluating the skin burns from laboratory standards. After this time the measured values were always significantly higher.

Since these atomic bomb burns are produced in such a short time it is improbable that evasive action would be effective in modifying their severity.

Severity of small and large area burns. No difference was seen in the severity of burns produced behind apertures ranging from 1.125 inches in diameter to a rectangle 2 by 5 inches in size. Subsequently 8 pigs were exposed behind a transite sheet having a central aperture 3 by 4.5 inches and four 0.75 inch circular openings 1 inch from each corner of the rectangular opening. No significant difference in severity could be detected by gross or microscopic examination between the small and large area burns in these animals.

Protective effects of fabrics. In the experiment designed to test the protective effects of herringbone twill, sateen, and serge, with and without underwear, 30 exposures were made using 10 white pigs. With but 1 exception no burns occurred behind any fabrics at any station. This was due to placing the animals at stations where the level of thermal energy was too low to cause burns through the fabrics. Subsequently laboratory data were obtained on the range of protection provided by these fabrics (5).

Effects of ionizing irradiation on thermal burns. There were 10 animals with lethal ionizing irradiation whose burns were observed during the interval before death. In 7 animals whose burn had progressed to the point of partial epithelialization, healing proceeded in spite of mortal irradiation sickness. But in 3 granulating, unhealed, biopsy wounds or burns became gangrenous and sloughed when signs of irradiation sickness appeared.

SUMMARY AND CONCLUSIONS

1. Thermal burn experiments were done at the detonation of atomic bombs in which ani-

mals were exposed behind clear quartz, timing shutters, filters, and fabrics in stations located at 14 different distances to cover the range from 1.1 to 43 calories per square centimeter. The results ranged from no burn to a char.

2. Radiation calorimeters were designed and placed in each station at tests to measure the total integrated energy and that passing through limiting filters. At subsequent tests measurements were made by others of the time resolution of the thermal energy incident on the exposed animals which provided for comparison of energy and burn severity.

3. Ninety-one white pigs, 8 black pigs, and 15 dogs were used as test animals. The white pigs proved the most satisfactory since fine gradations of color or coagulation of the skin were more readily detected.

4. Operational requirements made it necessary to place the animals in the stations many hours before they were exposed. Hence, a long-acting anesthetic without explosive hazards was necessary to assure anesthesia at the time of burning. Dial in urea-urethane injected intraperitoneally was satisfactory.

5. These animal lesions have demonstrated, for the first time, the characteristic gross and microscopic pathology of primary burns from the atomic bomb. The lesions closely resembled those caused by laboratory radiant energy sources.

6. In the laboratory, the time and intensity values of energy from the carbon arc have been obtained for burns of different degrees of severity in the white pig. The burns from the atomic bomb radiation could be assessed in terms of applied thermal energy by using these laboratory values.

7. No burns were produced in any animal through the filter transmitting only ultraviolet light.

8. The burns received behind filters transmitting visible and infrared rays were about equal in severity. Dark colored animals had a deeper burn than white ones.

9. No burns were produced by the initial flash during the first 20 to 25 milliseconds. Burns created by the second maximum or fire ball were equal in severity to those caused by the exposure to the total thermal pulse. At early tests, by means of a sliding shutter, the burn was found to be caused in the first 1/3 second after detonation of the bomb. At subsequent tests using a more refined timing shutter it was found that: (a) The skin burns produced in the period between 0.1 and 0.2 second after detonation were the most severe of any by a 0.1 second interval of the thermal pulse. (b) The major severity of thermal burns was attained within the first 0.3 second and the maximum severity within the first 0.5 second after bomb zero. (c) No burns were produced after 0.6 second if the skin was shielded prior to that time. These results indicate that evasive action is of little value.

10. There was good relationship between the measured thermal energy and that determined by evaluating the skin burns from laboratory standards during the first 0.2 second. After this time the measured values were always significantly higher.

11. No difference could be detected between the severity of the small and large area burns when sustained in the same animal or in different animals at the same station.

12. A few experiments were done in which fabrics were tested for their protective effect against burns from the thermal radiation of the atomic bomb. Many more experiments have been done in the laboratory to evaluate this protection from clothing.

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THE USE OF ACRYLIC IMPLANTS IN ONE STAGE RECONSTRUCTION OF THE MANDIBLE

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THE more recent advances in surgical technique, blood replacement, anesthesia, and antibiotics have made possible an increasingly effective attack on malignant diseases. This has been especially true in the field of surgery of the region of the head and neck where a greater variety of malignant lesions have become more approachable than was anticipated even a decade or two ago. At the same time this very accessibility has aggravated the major drawback to the expansion of this field, namely the cosmetic and functional deformity which is the concomitant of wide surgical removal. The reluctance of the lay public and a large segment of the medical profession to accept such deformity has frequently led to the adoption of substitute therapies such as irradiation or limited surgery in situations in which these modalities may not have constituted the treatment of choice. Although the primary goal must always be cure of the disease, nevertheless, the surgeon must make every effort to minimize cosmetic and functional deformity.

There is a large group of cases in which surgical resection of a segment of the mandible is a prerequisite to the best possible prognosis. It is most often this same group in whom the ultimate structural and functional result is the least satisfactory. During the recent war years considerable experience has been gained in the management and restoration of traumatic loss of portions of the mandible. Almost all of these methods, however, have had the disadvantage of requiring multiple staged procedures which are time consuming and, for the average civilian patient, economically unfeasible. For the patient with a cancer, where life expectancy is markedly foreshortened, it is all the more important to develop techniques of restoration to a comfortable and useful existence in the shortest possible time. From the standpoint of anatomy and physiology the ideal time for reconstruction is at resection, before soft tissue contractures and cicatrization have occurred. It would appear, therefore, that if a technique could be developed to accomplish such immediate restoration, the problems of morbidity and deformity would be greatly alleviated. We propose in this article to record our experiences which indicate that, in selected cases, such reconstruction is feasible.

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BACKGROUND

Many independent researchers have reported their approach to this problem and there is a growing body of references to reconstruction of the mandible using autogenous bone, homologous bone, ivory, stainless steel, vitallium, and, more recently, the inert plastics. The results reported have been as variable as the types of material used. It is generally accepted that, in carefully selected cases, a grafted autogenous bone will give uniformly satisfactory results. However, since the use of a living graft requires the presence of a well vascularized soft tissue bed and the virtual absence of contamination, it becomes apparent that only a relatively small number of mandibular defects lend themselves to this method. Even in these selected cases a disturbingly high incidence of delayed resorption, extrusion of the graft, or chronic osteomyelitis of the adjacent bone is observed. Furthermore, bone grafts have not been used very successfully for reconstruction of the temporomandibular joint when removal of

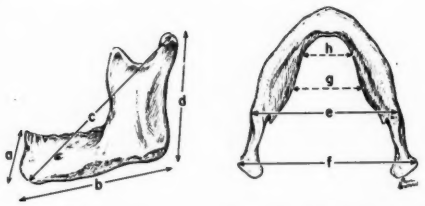


Fig. 1. Caliper measurements required for construction of prosthesis: *a*, superior-inferior dimension at the line of proposed transection, *b*, lower border of symphysis to the angle, *c*, lower border of symphysis to head of condyle, *d*, head of condyle to the angle, *e*, angle to opposite angle, *f*, head of condyle to head of opposite condyle, *g* and *h*, crest of the alveolar ridge to opposite crest at two arbitrary points measured intraorally from the midline of the alveolar ridge.

the head and neck of the mandible has become necessary.

To overcome some of the limitations and defects of the living graft, many efforts have been made to utilize nonreactive materials. The use of ivory or heterologous bone has produced disappointing results because of the reactivity of the implant and the difficulty of maintaining a stable union between the prosthesis and the mandibular fragments. Of the various metallic implants, vitallium appears to be the most acceptable according to Conley, since it is inert, allows replacement of the joint, and reattachment of the jaw muscles. However, these precast molds allow no adjustment for size, angulation, or contour so that the operation may have to be adapted to the prosthesis rather than the prosthesis to the operation.

It was our desire to select a material and develop a technique which would attempt to meet the following objectives: (1) lack of reaction to body tissues, (2) sufficiently light in weight to be functionally acceptable, (3) sufficiently strong to withstand normal activity and trauma, (4) adaptability to the specific surgical problem at hand, (5) reproduction of the physical and functional characteristics of the temporomandibular joint, (6) allow for the effective reattachment of muscle groups, (7) enable the construction of a self contained method of permanent fixation to the attached bone, (8) reasonable in cost, (9) feasibility of construction, and (10) clinically successful in restoring contour and function.

Of the materials available, it appeared that one of the synthetic plastics would lend itself best to the achievement of these objectives. Various types of inert plastic materials have been used as implants in different parts of the body with generally successful results. Of the various plastics, methyl methacrylate can be tolerated successfully by the body in a wide variety of situations including those requiring weight bearing and other types of stress and strain. Very little investigation has been conducted on plastic substitutes for the mandible. In 1946, Martin Lagos reported a two stage reconstruction of the resected mandible in a 17 year old girl with a periosteal fibrosarcoma of the symphysis. Reconstruction was accomplished with an acrylic implant held in place with stainless steel wires. In 1949, Adan reported a similar two stage reconstruction of the mandible from the sigmoid notch to the mental foramen. In 1950, Hector employed acrylic segments for replacement of the lower jaw in dogs but concluded that the procedure was impractical because of orocutaneous fistulization. Caorsi and his co-workers in 1950 reported variable results in a series of patients in whom acrylic implants were made.

PREPARATION OF THE PROSTHESIS

Any experienced prosthodontist should be capable of constructing a mandibular implant to replace an operative defect. Dental technicians, already familiar with the handling of acrylic, should be capable of constructing such a prosthesis according to the dentist's requirements. Accordingly, the services of the Dental Department of this hospital were solicited for the development of this phase of the problem. After a series of trials, there has gradually evolved a technique which has answered our objectives in nearly all instances.

The technique has as its chief aim the production of a nonreactive acrylic prosthesis whose measurements accurately reproduce those of the mandibular segment to be removed. Any desired segment of the mandible may be produced by modifying the steps in the technique to be outlined which describes reproducing a complete half of the mandible.

The reproduction of any mandibular segment requires the careful recording of certain

dimensions which are obtained directly from the patient by caliper measurement under local anesthesia (Fig. 1). In addition, the angle formed by the horizontal and ascending rami must be accurately calculated. Direct measurement of this angle on the patient has proved to be inaccurate, especially in the presence of a prominent parotid gland. Therefore, to supplement and confirm the direct measurements, the following roentgenograms are taken: (a) submental vertex films showing the curvature of the mandible and the distance between the rami at the angles, (b) lateral views of the angle, and (c) intraoral and occlusal dental films at the site of transection.

When disarticulation is contemplated, laminagrams of the temporomandibular joint are also desirable to show the contour and size of the condyle and its relationship to the coronoid process. All roentgenograms excepting the intraoral occlusal and laminagrams are taken at a distance of 72 inches to minimize distortion. The occlusal film is taken at approximately 20 inches.

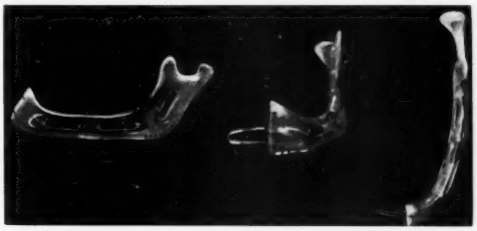
To serve as a starting point for all cases of mandibular reconstruction, 3 standard latex molds are prepared from 3 mandibles, 1 considered to be average in its overall dimensions, 1 smaller, and 1 larger. Wax is softened and poured into the molds forming 3 casts identical to the 3 selected mandibles. The wax cast which most closely approximates the patient's recorded measurements is selected. This cast is then altered to coincide with these measurements. The cast is first cut at the proposed site of transection; then precise reproduction of the angle of the mandible is accomplished by cutting the wax and altering the angle on the wax cast to the exact measurement as previously recorded by direct measurement and by x-ray examination (Fig. 2).

Some of the bulk of the horizontal and ascending rami is then decreased by cutting away the wax along the superior and inferior borders to avoid undue tension when the soft tissues are resutured over the implant. This narrowing is done only in the midportion of the prosthesis leaving the dimensions unaltered at the point where the prosthesis joins the remaining mandible.

a b c d

Fig. 2. Various stages in the preparation of the prosthesis. a, Latex mold of a "standard" mandible. b, Wax cast from latex mold. c, Wax cast after alteration to patient's measurements and implantation of locking device. d, Completed prosthesis after investment of cast and packing with acrylic.

In order to effect junction with the remaining fragment of the mandible various types of attachments were tried. In the early restorations, 2 flat stainless steel pins were embedded in the prosthesis and inserted into the cortex of the remaining mandible. This technique was later abandoned in favor of one designed to give even greater stability. A fenestrated, wedge-shaped insert of acrylic was formed on the abutting end as an extension of the prosthesis. At the time of resection, the medullary cavity of the remaining mandible is curetted sufficiently to permit the impaction of the acrylic insert. As the prosthesis is inserted, the medullary curettings are impacted into the open center of the insert. It is anticipated that consolidation of the fragments about the



a

b

Fig. 3. Completed prostheses. a, Restoration of hemimandible. Note narrowing of ramus to minimize soft tissue tension. Large slots allow ingrowth of soft tissues. Drill holes permit attachment of muscles and wiring of implant to mandible. Locking device of stainless steel allows for adjustments in curvature and torque. b, Restoration of anterior segment of mandible. Note details of double locking device cast in acrylic.

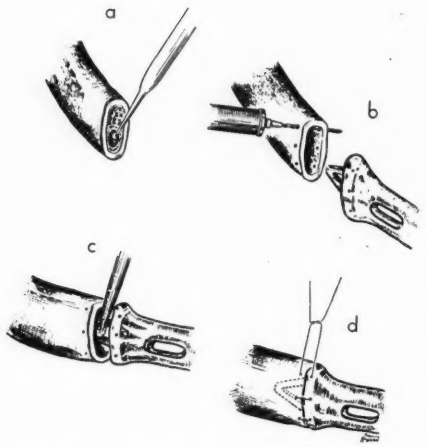


Fig. 4. Technique of fixation of prosthesis to mandibular fragment. a, Medullary cavity is curetted to allow snug fit of locking device. b, Three drill holes are placed opposite the holes in the prosthesis. c, Medullary bone fragments are packed into fenestrated opening as locking device is impacted. d, Fixation with No. 28 stainless steel wire sutures.

locking device would produce, in effect, a bony union between the prosthesis and the mandible. In later cases this device was constructed of flat stainless steel to permit slight adjustments at the time of insertion, should the apposition not be perfect. This stainless steel locking device is imbedded in the end of the wax cast, care being taken to follow both the curve and angulation of the remaining mandible to avoid torque.

The finished wax cast is now invested, packed with methyl methacrylate polymer in granular form, and mixed with a liquid monomer. This is processed under pressure at a temperature of 158 degrees for 2½ hours and then of 212 degrees F. for 21½ hours. After curing, the prosthesis is cleaned and polished (Fig. 3a). Three holes are drilled at the transected end of the prosthesis to facilitate its fixation by wires through similar perforations in the remaining mandibular fragment. Perforations are also made at the inferior border of the angle and top of the coronoid process for attachment of the masseter, internal pterygoid, and temporalis muscles. Should the restoration include the symphysis, similar perforations are drilled at the inferior border of the symphysis for attachment of the geniohyoid muscle. In earlier cases the prosthesis was roughened over the areas of muscle attachment. Later, small perforations were drilled throughout the entire prosthesis. However, it has since been determined that better results are achieved when large apertures are cut in the prosthetic restoration so that the openings are allowed to become occupied with fibrous connective tissue.

When the removed segment of mandible does not include the joint, construction of the prosthesis is more simple. Two locking devices are constructed (Fig. 3b) for fixation of the implant to the transected mandibular fragments. When replacing the anterior segment of the mandible, it is desirable to recess the symphysis at least 1 centimeter to avoid undue tissue tension.

Prior to surgery the prosthesis is sterilized by scrubbing with a detergent such as pHisoHex, followed by immersion for 20 minutes in a 1/1000 solution of zephiran (benzalkonium chloride).

OPERATIVE TECHNIQUE

No attempt will be made to describe operative procedures in detail except as they apply to the use of the prosthesis. All patients receive endotracheal anesthesia administered through a preliminary tracheotomy. In general, wide removal of the primary tumor is accomplished in continuity with the mandible and regional lymph nodes. As a rule the radical neck dissection is carried out first, basing the specimen on the segment of mandible proposed for resection. The extent of the mandibular resection is determined by the size, type, and contiguity of the primary growth, giving a minimal clearance of 2 centimeters. If the resected mandible includes the angle, we have preferred to disarticulate at the temporomandibular joint rather than risk the possibility of an unstable junction of the prosthesis with the thin ascending ramus. The floor of the mouth is entered from beneath the mandible at the proposed site of transection.

The prosthesis is brought into the field to assist in marking on the mandible, in gentian violet, the precise site of transection. The mandible is then divided with a Gigli saw. If

Fig. 5. Case 1. a and b, Before and 13 days after surgery. c, Prosthesis in the operative field assists in localizing the line of resection. d, Prosthesis in place just prior to impaction and suture with steel wire.

disarticulation is indicated, the massester, internal pterygoid, and temporalis muscles are detached with a periosteal elevator and the joint exposed. A vertical incision is made in the capsule which is reflected and separated by sharp dissection from the neck of the mandible. When the mandibular segment has been freed, removal of the primary lesion is then completed.

The prosthesis is again brought into the field and the medullary cavity of the transected mandible is curetted to a degree sufficient to permit a snug fit of the "male" locking device (Fig. 4). The curettings are preserved and replaced in the fenestrated portion of the locking device when the prosthesis is finally impacted in position. It is anticipated that consolidation of these fragments will form a

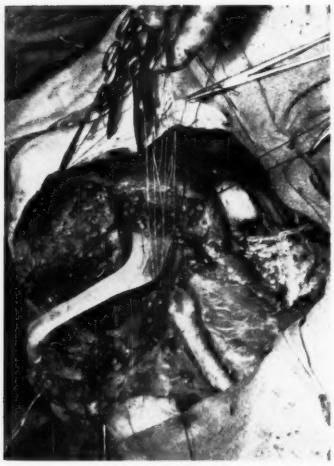


Fig. 6. Case 2. Operative view showing final steps in implanting prosthesis which extends from the left temporomandibular joint to the right mental foramen. Wire sutures have been placed for reattachment of the masseter, internal pterygoid, and geniohyoid muscles.

bony bridge to lock the prosthesis solidly in place. Additional and immediate fixation is provided by drilling 3 holes through the bony mandible and securing the prosthesis with 3 interrupted sutures of No. 28 stainless steel wire.

If the prosthesis includes the condyle, this structure is held in place by resuturing the joint capsule over the neck of the implant with several interrupted sutures of fine black silk. Articulation is maintained by the subsequent soft tissue closure. The oral cavity is closed and the wound thoroughly irrigated with normal saline solution to minimize contamination by saliva. The operator and assistants change gowns and gloves and the operative field is redraped. When indicated and feasible, the temporalis, internal pterygoid, masseter, and geniohyoid muscles are sutured to the appropriate perforations in the prosthesis. Soft tissues and skin are closed without tension over the prosthesis. Drainage of the deep structures is carried out routinely.

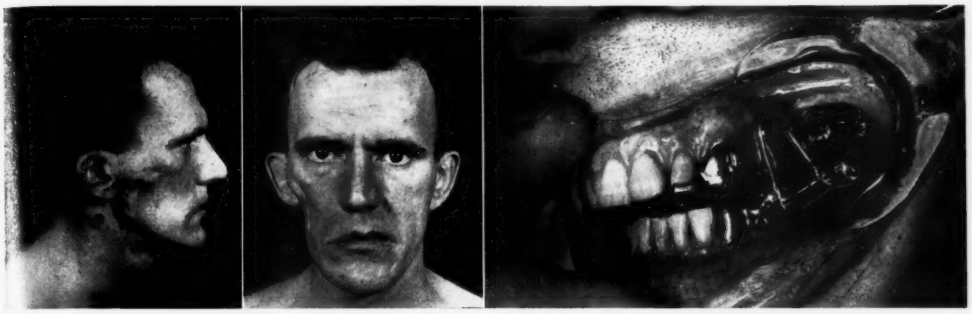
Operating time varies from 4 to 11 hours, depending upon the magnitude of the resection. About 30 minutes are required for the actual implantation of the prosthesis. Blood is replaced as lost, requirements varying from 1,000 to 3,500 cubic centimeters. Our choice of suture material has varied although, in general, mucous membranes are closed with fine chromic catgut, while fine silk is used for hemostasis and soft tissue closure. Penicillin and streptomycin are given routinely preoperatively and postoperatively until the wound has healed. In this series of cases there were no wound infections and no operative mortality.

CASE REPORTS

CASE 1. The patient was a 53 year old white male with an ulcerating lesion of the left posterior inferior alveolar ridge of 3 months' duration. The lesion measured 2 by 2 centimeters and involved, by contiguity, the buccal mucosa, alveolar ridge, and anterior tonsillar pillar, and on biopsy proved to be an epidermoid carcinoma, grade III. There was a firm, metastatic deposit in the left subdigastric region. Because of the location of the lesion it was decided to resect the left mandible from the temporomandibular joint to the mental foramen. Measurements were taken and an acrylic prosthesis constructed by the method described. On February 25, 1952, a preliminary tracheotomy was performed and 2 days later the lesion was widely resected in continuity with the mandible and a left radical neck dissection. There was extensive, concealed, metastatic disease in the upper deep jugular nodes. The prosthesis was inserted and closure of the oral mucous membrane and skin was accomplished without any tissue tension. The wound healed primarily and he was discharged 3 weeks after the operation, able to talk and swallow very well (Fig. 5). The patient subsequently developed recurrent disease in the left neck and expired of hemorrhage 3½ months postoperatively.

Despite the failure to cure the advanced disease, the prosthetic reconstruction of the mandible yielded a most satisfactory result. Although there was a slight drift of the mandible to the right, the cosmetic result was good and the functional result was considered excellent since the patient could chew, swallow, and talk without difficulty or pain up to the time of his death.

CASE 2. A 51 year old white male with a 5 month history of soreness presented an extensive ulcerating epidermoid carcinoma of the entire left alveolar ridge from the angle to the symphysis and spilling out to involve the floor of the mouth and the left tongue border. On March 7, 1952, a preliminary tracheotomy was performed, and on March 12 the patient underwent a left hemiglossectomy and left radical neck dissection in continuity with the mandi-



a b c

d e f

Fig. 7.

Fig. 7. Case 3. a, Recurrent carcinoma of right parotid beneath skin graft. Dark spot designates site of metastasis in posterior cervical lymph node. b, Preoperative frontal view. Note partial facial paralysis. c, Onlay type of guide plane to maintain articulation and to prevent drift of the mandible. d, Operative view. Note area of skin sacrificed over cheek and jaw. Neck dissection completed, specimen excised including skin, parotid, facial nerve, zygoma, and mandible. Spinal accessory nerve has been swung upward behind the prosthesis, split, and anastomosed to the ophthalmic and buccal terminal branches of the facial nerve. e, After closure showing exposed prosthesis and skin defect to be covered by thoracoacromial pedicle flap. f, Twelve days after operation. Note complete facial paralysis.

Fig. 8. Case 3. Lateral and frontal views 12 months after operation. Complete facial paralysis has been helped by a fascial sling and canthoplasty. Jaw function is excellent.

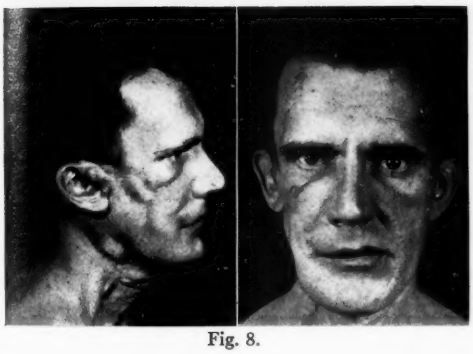


Fig. 8.

ble and the floor of the mouth. The resected mandible extended from the left temporomandibular joint to the right mental foramen. An acrylic prosthesis was inserted (Fig. 6) and closure accomplished under some tension. The postoperative course was uneventful until the third postoperative week when two small areas of separation of the suture line appeared between the tongue and buccal mucosa exposing the prosthesis in the floor of the mouth. These were closed with interrupted sutures under local anesthesia and thereafter remained healed. The patient was able to swallow well and talked with fair enunciation at the time of discharge.

He was readmitted 3 months postoperatively with a tumor recurrence in the left submental region. Subsequently, the tumor fungated and a sinus tract was noted to extend up to the prosthesis in spite of which there was remarkably little evidence of in-

fection. Palliative deep x-ray therapy was administered and the patient expired 7 months after surgery.

Here again, radical surgery failed to control the disease yet prosthetic restoration was effectively accomplished with benefit to the patient. The cosmetic result was less than satisfactory in this instance because errors in preoperative measurements resulted in an oversized prosthesis. Modifications of the technique have since avoided this error. In spite of the asymmetrical mandible, the functional and symptomatic response was good.

CASE 3. A 36 year old white male first noted a lump in front of the right ear in 1943 nine years prior to admission. The mass was excised, promptly recurred, and was again excised several months later. A third recurrence was excised and reported as a parotid carcinoma. In 1944, the fourth recurrence was treated by wide excision and skin grafting at the Walter Reed Hospital, followed by radium and deep x-ray therapy. In 1947, local excision of a recurrent nodule was reported as adenocystic carcinoma of the parotid. In 1951, at this hospital, he had a wide excision of a recurrent tumor in the same area. The most recent admission was in January 1952 nine years after the onset of his disease, with his sixth local recurrence. Examination revealed a hard nodule 1.5 centimeters in diameter immediately beneath the skin graft, and adherent to the zygoma and ascending ramus of the mandible (Fig. 7a). There was a 1 centimeter hard lymph node in the upper posterior neck densely adherent to the skin. A peripheral right facial paralysis was present (Fig. 7b).

Preliminary preparation included the construction on an onlay type of guide plane (Fig. 7c), an acrylic implant (Fig. 7d), a right thoracoabdominal tube (Fig. 7e), and a tracheotomy. On March 19, 1952, an operation was performed consisting of a right radical neck dissection in continuity with a block dissection of a large segment of involved skin, parotid gland, zygomatic arch, and the mandible from the temporomandibular joint to a point 3 centimeters anterior to the angle. The right facial nerve was sacrificed and the spinal accessory nerve anastomosed to the ophthalmic and buccal branches of the facial nerve (Figs. 7d, e). The acrylic prosthesis was inserted and the wound closed leaving a large defect which was covered by detaching and implanting the thoracoacromial tube pedicle. Total operating time was 11½ hours and the patient received 3,000 cubic centimeters of blood. Pathologic examination revealed adenocarcinoma of the parotid with invasion of the masseter muscle and metastasis to the posterior cervical lymph nodes.

The postoperative course was complicated by a lung abscess which cultured Friedländer's bacillus but which responded promptly to chloromycetin and postural drainage. The detachment of the thoracoacromial tube (Fig. 7f) was carried out in stages with a complete take of the graft and he was discharged 13 weeks postoperatively. Although there was a slight return of facial nerve function. the paralytic deformity persisted and was corrected by a fascial sling support to the mouth and a cantholplasty (Fig. 8). Sixteen months following surgery there is no evidence of recurrence and the patient has excellent function of the jaw. He can chew, swallow, and talk without any difficulty.

This case illustrates a teamwork effort which included the dental surgeon, otolaryngologist, plastic surgeon, and general surgeon. The combination of radical excisional surgery with immediate functional and anatomic restoration resulted in diminished morbidity and the maintenance of facial contour and jaw function.

CASE 4. A 52 year old white male presented a 4 week history of an ulcer of the floor of the mouth. The lesion was in the midline, measured 2 by 3 centimeters in size, and extended from the frenulum of the tongue to the alveolar ridge. Biopsy revealed epidermoid carcinoma, grade II. After preliminary tracheostomy, resection of the anterior tongue, floor of the mouth, and bilateral suprahyoid neck dissection were carried out on May 20, 1952 in continuity with the anterior segment of the mandible. An acrylic prosthesis was implanted extending from the right to the left mental foramina. The patient was discharged 3 weeks after operation with the wound healed and with good talking and swallowing function (Fig. 9).

Two months later the skin broke down over the midline exposing the symphysis of the prosthesis. The exposure was obviously the result of contracture of the tissues and the pull of the tongue muscles which drew the skin taut on the prosthesis until breakdown occurred. Secondary closure was accomplished on September 16, 1952 by sliding skin flaps and the transplantation of the sternocleidomastoid muscle to fill in the dead space. Closure was successful for 4 months when further contracture and muscle pull again produced exposure of the prosthesis in the midline. The implant was removed on January 23, 1953 and the patient has remained well since.

Undoubtedly the sacrifice of muscle of the anterior tongue and floor of the mouth resulted in undue tension and muscle pull after implantation of the prosthesis. The cosmetic and functional results were excellent although relatively short lived.

CASE 5. This 59 year old white male presented an epidermoid carcinoma of the anterior floor of the mouth almost identical to that in Case 4. The lesion

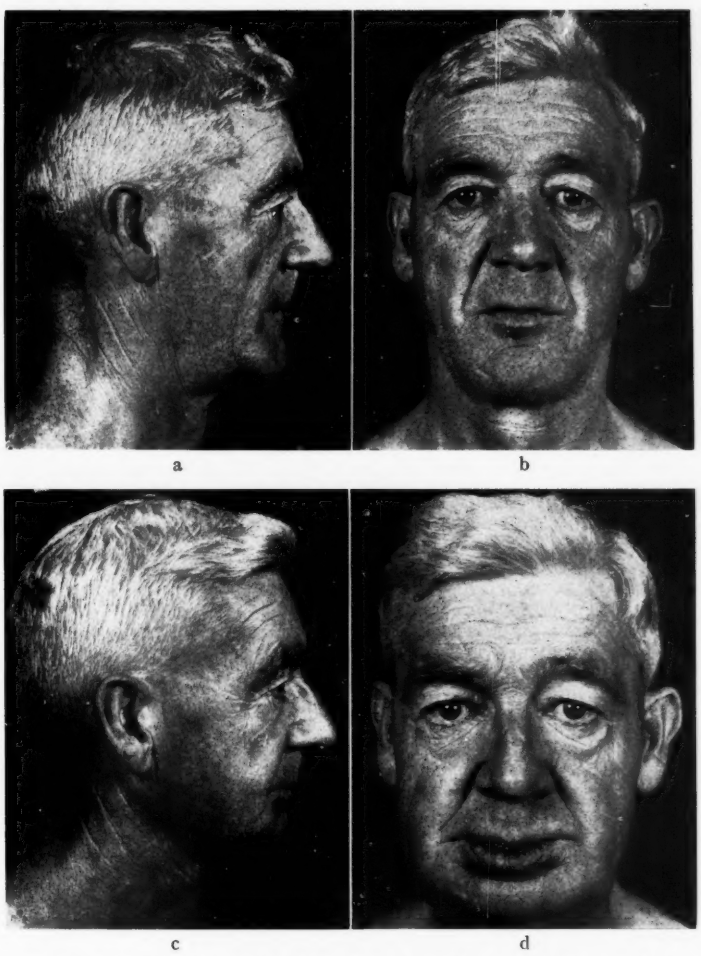


Fig. 9. Case 4. Carcinoma of anterior floor of mouth. a and b, Preoperative appearance. c and d, Twenty days after resection of anterior segment of mandible and acrylic restoration. Postoperative edema is still present.

was 3 by 3.5 centimeters in size and extended from the frenulum of the tongue to the alveolar ridge in the midline. On June 11, 1952, after preliminary tracheostomy, the patient underwent resection of the anterior tongue, floor of the mouth, mandible, and bilateral radical neck dissection. The resected mandible was replaced by an acrylic prosthesis (Fig. 3b) extending from the right to the left mental foramina.

The wound healed primarily and the patient had a very satisfactory cosmetic and functional result which lasted 12 months, after which time the prosthesis became exposed in the midline, again as the result of gradual contracture of the soft tissues and the pull of the tongue muscles. The prosthesis was removed on June 9, 1953 after which the wound healed promptly. The patient was free of recurrent disease 13 months postoperatively.

Again a very satisfactory cosmetic and functional result was obtained with an anterior implant but it lasted only 1 year before the prosthesis became exposed.

CASE 6. A 42 year old white male presented an extensive carcinoma of the right inferior alveolar

ridge, invasion of the mandible, and a fungating metastatic deposit 7 centimeters in diameter in the right submaxillary region. The patient received 7,200 roentgens of deep x-ray therapy with considerable regression in the size of the lesion. During this period a right thoracoacromial tube was prepared in stages. On July 23, 1952, tracheostomy was performed followed by resection of the mandible from the right temporomandibular joint to a point 1 centimeter to the left of the midline. This was accomplished in continuity with a right radical neck dissection and a large area of skin which was involved with the tumor. Immediate reconstruction of the mandible was accomplished with the aid of an acrylic implant which was covered under moderate tension by the utilization of the thoracoacromial tube.

Postoperatively, there was necrosis of the skin flaps and the periphery of the tube pedicle with exposure of the prosthesis which, accordingly, was removed 8 days later, and the defect was covered with split thickness grafts.

In retrospect, a prosthesis should not have been used in this case because of the extensive soft tissue excision necessitating closure under tension.

CASE 7. A 64 year old white male presented a 1.5 centimeter ulcerating lesion on the anterior alveolar ridge just to the right of the midline. A biopsy revealed epidermoid carcinoma, grade I. On September 10, 1952, after preliminary tracheostomy, the patient underwent resection of the anterior floor of the mouth and mandible with bilateral supraomohyoid dissection. The mandible was reconstructed with an acrylic prosthesis extending from the right to the left mental foramina. On the fifth postoperative day the suture line in the anterior floor of the mouth retracted to expose the prosthesis. It was believed that tension, due to sacrifice of soft tissues, was responsible for the breakdown. On October 15, 1952, the defect was closed by simple suture. This procedure failed and 3 weeks later it was repeated with success. The patient had a good result cosmetically and functionally for 2 months, when again the prosthesis became exposed in the anterior mouth. Further surgery was contemplated, but the patient suddenly expired on January 30, 1953 of a coronary thrombosis.

Again tissue tension, resulting from the sacrifice of soft tissue, was responsible for breakdown of the suture line. Even while the prosthesis was exposed in the mouth, there was no evidence of reaction of the adjacent mucous membrane nor of osteomyelitis of the mandible. The functional and cosmetic result was very good in spite of the exposure of the prosthesis.

CASE 8. A 65 year old white male presented a painless swelling of the left jaw of 5 years' duration. On examination there was a large, bony hard, globular tumor of the horizontal ramus of the left mandible. The tumor had broken through the alveolar ridge into the mouth cavity. Roentgenograms revealed an expansile loculated tumor of the mandible with an intact bony capsule except for the point of break through along the alveolar ridge. The "soap bubble" loculations extended up the ascending ramus of the mandible. Biopsy was reported as adamantinoma with malignant change. On September 19, 1952, after preliminary tracheostomy, the left mandible was resected from the temporomandibular joint to the symphysis mentis. Total restoration was accomplished with an acrylic prosthesis (Fig. 10). The wound healed promptly and he was discharged 1 month postoperatively with good restoration of contour and jaw function. Eleven months later there was no evidence of recurrence; the patient could speak, chew soft foods, and swallow without difficulty and experienced no pain or discomfort in either temporomandibular joint. The mucous membrane over the prosthesis remains completely healed and shows no sign of breakdown.

This case illustrates the feasibility of immediate reconstruction of the mandible with a minimum morbidity and a highly satisfactory result from a cosmetic and functional standpoint.

DISCUSSION

In properly selected cases, immediate restoration of the surgically resected mandible by means of an acrylic prosthesis appears to be both feasible and desirable. With the assistance of any well trained prosthodontist and a dental technician, the production and implantation of an acrylic prosthesis are within the reach of any general surgeon who performs radical surgery of the head and neck. No special facilities are required other than those normally found in the average dental laboratory. Whenever there are sound articulating teeth on the contralateral side, the use of a guide plane is considered advisable to assist in the continued maintenance of articulation and the prevention of mandibular drift.

Our limited experience would indicate that restoration of the lateral segments of the mandible, including replacement of the temporomandibular joint, can be expected to give uniformly satisfactory results, both cosmetic and functional. Immediate restoration of facial contour has been of immense psychologic

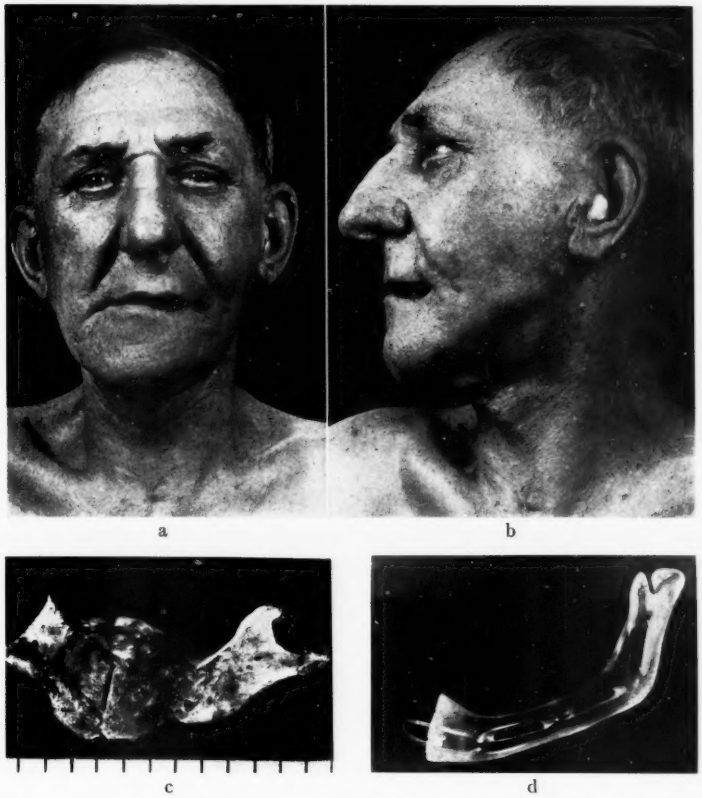


Fig. 10. Case 8. Adamantinoma of mandible. a and b, Appearance 12 days following total restoration of left mandible. c, Operative specimen. d, Acrylic implant.

benefit to patients who would otherwise be confronted with the serious problem of deformity. Talking or swallowing are not impaired beyond the loss occasioned by surgical resection. Actually, the implant enhances the remaining functional capacity by stabilizing the mandibular fragment and affording a new site for muscle insertion. In no cases has temporomandibular joint pain been noted except for a transient episode in 1 patient (Case 3) which was promptly corrected by adjustment of the guide plane. In all cases the ability to chew has been limited only by the extent of remaining dentition. All have been able to eat soft foods, and 2 more venturesome patients have resumed a normal diet without apparent harm.

On the contrary, our experience with replacement of the anterior segment of the mandible has been less than satisfactory. In all 3 cases reported the prosthesis has eventually become exposed either through the skin of the midline of the chin or along the intraoral suture line. In each instance it was necessary to remove substantially large amounts of the musculature of the tongue and floor of the mouth. It is our belief that the resultant tension and scar tissue contracture is responsible for the gradual production of pressure on the overlying skin or mucous membrane, which eventually causes necrosis and breakdown. We believe, however, that the technique would be suitable for cases in which simple resection of the mandible is indicated without

the loss of the surrounding soft tissues. In such a situation the implantation of the prosthesis is a simple technical matter and should result in prolonged maintenance of jaw function and facial contour. Simple dehiscence of the mucous membrane should not necessarily require removal of the prosthesis and efforts should be made to free the flaps, close the dead space, and resuture the mucosa. If breakdown of the skin occurs sliding flaps should be attempted, and if not successful a tubed pedicle graft may be used to cover the defect.

SUMMARY

A detailed technique is presented for the immediate restoration of the surgically resected mandible utilizing custom built prostheses of acrylic (methyl methacrylate). Eight cases are presented in which this technique was utilized. Results were poor in 1 case, partly successful in 3 cases, and excellent in 4 cases. The indications for, and the limitations of the technical method are discussed in detail. The benefits to be derived from the use of a prosthetic implant are sufficiently great to warrant their use in any case of surgical resection of the mandible unless the procedure is of such a magnitude and the destruction of surrounding soft tissues so great that one could not anticipate closure around the prosthesis without undue tension.

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A METHOD FOR THE SURGICAL CORRECTION OF MITRAL INSUFFICIENCY

I. Preliminary Considerations

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THE surgical treatment of mitral insufficiency remains one of the more challenging problems confronting the cardiovascular surgeon today. Many ingenious techniques have been devised in attempts either to reconstruct the valve cusps or to create other means of restoring valve function. Outstanding examples of such endeavors are the suggestions of Murray, Wilkinson, and McKenzie who used vein grafts to replace damaged cusps and Templeton's experimental attempts at the actual reconstruction of the cusp with flaps of pericardium or vein wall sutured in place of the damaged or wasted valve leaflets under direct vision. Bailey, O'Neill, Glover, and others (2, 3) and, more recently, Logan and Turner have constructed "slings" or flutter-valves fashioned of pericardium placed within the ventricle immediately beneath the atrioventricular orifice. Henderson and Glover (4, 6) and, subsequently, Moore and Shumacker showed early that grafts of tissues such as those used in the techniques described do not retain the anticipated desirable properties. Within a short time they are transformed into useless fibrous cords devoid of resiliency and acting as immobile struts bridging the ventricular lumen. Furthermore, they represent a locus for thrombosis formation and ofttimes actually create an obstruction to blood flow if they become swollen and edematous soon after placement. Thus, neither the early or late effects of this method warrant its further consideration.

O'Neill and Glover (10) have invaginated the enlarged left atrial appendage into and through the valve ring, anchoring its inverted tip to the lateral wall of the ventricle in the hope of providing a buttress against which the aortic (anteromedial) cusp of the mitral valve can close. This procedure is effective only to the extent to which that cusp has retained its motility and, therefore, is not routinely applicable. Harken has devised various plastic prostheses to obtain the same general effect. Such prostheses are intended as substitutes for the loss of valve substance. A valve substitute of this type cannot be made to function with more than very temporary, even questionable, efficiency; the mortality for its technical introduction is too high and the undesirability of intracardiac foreign material is obvious. Recently Bailey (1) has attempted to suture the mitral leaflets to each other in order to obliterate the incompetent portion of the valve orifice. This technique necessitates the passage of a strip of pericardium through the body of the leaflets and thus entails a risk of tearing these structures. It also requires that a segment of the pericardial strip be stretched transventricularly with its terminus embedded in the myocardial wall and thus it is subjected to the atrophic changes which have been mentioned. In addition, if the loss of valve substance is great, complete elimination of the regurgitation would be accompanied by the production of too much stenosis. These reasons, together with the trauma and appreciable mortality entailed in its performance, suggest that other avenues must be investigated.

All of the methods mentioned are based on one general principle: namely, to supply substitutes for the *absolute* loss of valve substance, admittedly the most difficult feature of the lesion. It is our purpose to approach the problem from an entirely different aspect: namely, to decrease the size of the orifice

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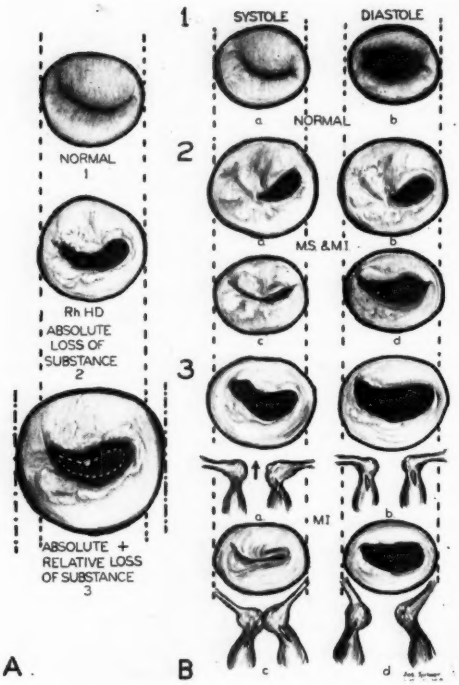

Fig. 1. A-1, Normal mitral valve closed. A-2, Rheumatic valvular disease may produce mitral insufficiency by the *absolute* loss of valvular occluding substance which results from scar contracture. At this stage, enlargement of the atrioventricular ring does not play a significant role. A-3, Once regurgitation is present as a result of absolute loss of substance, compensatory myocardial hypertrophy and dilatation lead to a progressive enlargement of the atrioventricular ring and, therefore, a progressive *relative* loss of occluding substance with an attendant increase in the amount of regurgitation. B-1, The normal mitral valve in systole (a) and in diastole (b). B-2, The typical case of mitral valvular disease presents a picture of combined stenosis and insufficiency the degrees of which may vary greatly. The stenosis is the result of fusion of the cusps, usually at the anterolateral commissure which prevents adequate opening (b). The insufficiency is due to the rigidity of the posterior portion of the cusps which form a "tear drop" orifice incapable of closing (a). The regurgitant factor is further aggravated by dilatation of the atrioventricular ring. If the stenotic factor is corrected by commissurotomy the valve is rendered capable of opening adequately but in a large number of cases the restoration of motion may not be enough to allow competent function. If, in addition to the commissurotomy, the size of the ring is reduced (c and d) two things can be accomplished: the size of the ring is limited thus preventing further relative loss of substance, or ideally the ring is reduced in size sufficiently so that it can be occluded by available valve substance. B-3, In so-called "pure" mitral insufficiency complete closure of the valve in systole is impossible (a), because of absolute as well as relative loss of substance. The pull upon the valve leaflets by the enlarged ring has an effect comparable to that of an embroidery frame upon the cloth; the shortened chordae tendinea place additional limits on valve motion much as taut lines restrain a sail, both of these mechanisms further limit the competence of the occluding elements. The opening of the valve (b) presents no problem. If the size of the ring is reduced the effect is multiple. The area to be occluded is made more compatible with the amount of valve substance present and the valve motion is enhanced by virtue of the release of tension on the leaflets and relaxation of the chordae (c and d).

which the limited valve tissue is vainly attempting to occlude.

Mitral insufficiency is the result of several factors all of which act upon the valvular elements in various combinations and at various times in the developmental cycle of the pathologic process. The pathogenesis of rheumatic valvular disease is well known. The initial inflammatory lesion leads to cicatricial deformity which, in the end, results in the absolute loss of substance of the leaflets. The extent of this loss depends upon the degree of contraction by scar, of loss of motility by thickening, calcification, or fusion of portions of the cusps, as well as, additional limitation of motility by the restraining action of shortened chordae tendineae. These phenomena are responsible for the production of valvular stenosis or insufficiency. The common lesion seen clinically is a partial stenosis with which there is associated some degree of regurgitation. The clinical manifestations of the disease are determined by the degree to which one or the other of these pathologic states predominates. When mitral insufficiency is dynamically significant the compensatory changes necessary to maintain an adequate cardiac output eventually lead to dilatation and hypertrophy of the left ventricular myocardium, which is accompanied by corresponding enlargement of the atrioventricular ring, that is, there is a *relative* loss of valvular occluding substance (Fig. 1A). The tremendous enlargement of the left atrium, which is so frequent in cases of mitral insufficiency, may, perhaps, also contribute to the increased size of the mitral ring. The increased regurgitant volume resulting from these changes creates a need for bringing into play additional compensatory reserve of the myocardium which

in turn undergoes further dilatation and hypertrophy. The vicious cycle continues to its inevitable conclusion by exhaustion of myocardial reserve and death. It can be assumed that once the cicatricial changes in the valvular tissues reach a peak the evolution of the picture of left ventricular failure depends on the progressive increase in regurgitation resulting from the progressive relative loss of substance which, in turn, produces added left ventricular strain. It seems reasonable, therefore, to suppose that if the progressive enlargement of the atrioventricular ring can be halted, the vicious cycle can be broken and the compensatory mechanisms of the heart can be protected. Even better, if the area of the atrioventricular ring can be reduced sufficiently to decrease the discrepancy between the absolute amount of valve substance remaining and the absolute and relative amounts lost, the degree of regurgitation can be greatly diminished or perhaps eliminated entirely. It is well known that the size of the mitral ring can be reduced to some extent without the production of significant alteration in the hydrodynamics of the pulmonary circulation or in the function of the right heart. It is to be expected that, in a number of cases, the management of the lesion would include initial commissurotomy in order to release fused cusps which are potentially capable of restored function (Fig. 1B).

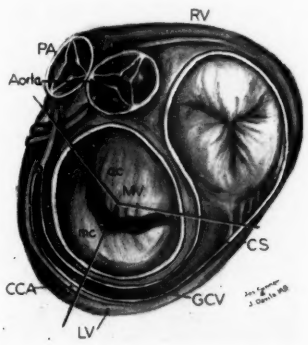

Fig. 2. A view into the atrioventricular rings in a heart in which the atria have been removed, and the coronary sinus and great cardiac vein unroofed. *PA*, Pulmonary artery and valve; *RV*, right ventricle; *acMV*, aortic (medial or septal) cusp of the mitral valve; *mc*, mural cusp of the mitral valve; *CCA*, circumflex coronary artery; *LV*, left ventricle; *GCV*, great cardiac vein; *CS*, coronary sinus. The radial lines arising in the center of the mitral ring indicate the zones (see text).

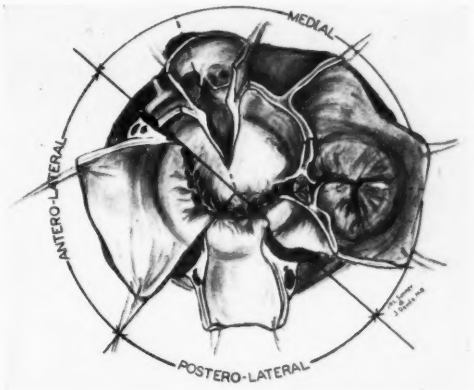

Fig. 3. A view into the atrioventricular rings similar to that in Figure 2 but with the atrial wall left attached to the rings. The heavy radial lines mark the zones. The dotted lines indicate sections through the ring at points adjacent to the aorta (dotted line at 11:00 o'clock) and to the interatrial septum (dotted line at 3:00 o'clock). In these segments the periannular space is all but obliterated. The other sections demonstrate the anatomic relationships of the ring in the corresponding zones.

The best means of accomplishing our purpose appears to be the placement of a constricting ligature or purse-string suture around the atrioventricular ring. It is interesting to note that many investigators have attempted to produce mitral stenosis in animals in this or very similar ways. However, no suggestion has been made heretofore of the possible use of such a device for the treatment of mitral insufficiency. This mechanical constriction seems particularly suitable for our purposes since a true valvular stenosis cannot be produced by this means. Other methods of reducing the ring have been used in the experimental production of stenosis. These, however, entail actual tissue injury which induces a true cicatricial deformity of variable degree which cannot be accurately controlled.

In order to explore the technical difficulties which might be encountered in the placement of a circumferential constricting suture at the atrioventricular ring a series of dissections on 18 fresh human hearts, obtained at necropsy, were undertaken. The anatomy of the atrio-

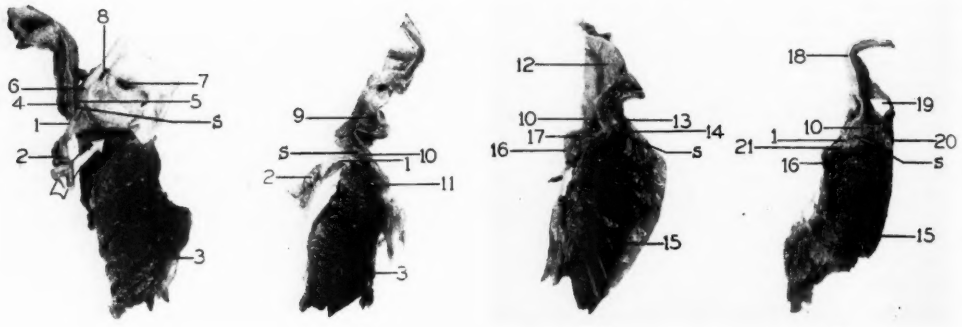

Fig. 4. These photographs of sections through the mitral valve rings demonstrate in more detail its anatomic relationships. A, A section through the septal cusp, the ring and the aortic valve. The arrow indicates the left ventricular outflow tract. *1*, Valve ring; *2*, septal leaflet; *3*, interventricular septum; *4*, base of the left atrial appendage; *5*, pericardial reflexion forming the grooved floor of the transverse sinus; *6*, wall of the left anterior sinus of Valsalva; *7*, ostium of the right coronary artery; *8*, ostium of the left coronary artery. B, A section through both atrioventricular rings at a point in the posterior basal region of the interatrial septum. *9*, Interatrial septum; *10*, the periannular space lies here limited by the atrial walls as the fibers separate to insert into the corresponding fibrous rings by the rings themselves and by the interventricular septum; *11*, tricuspid valve ring. C, This section cuts the ring at the anterolateral commissure. *12*, Wall of the left atrium and appendage; *13*, circumflex coronary artery near its point of origin; *14*, great cardiac vein at point of branching downward anteriorly to become the anterior cardiac vein; *15*, left ventricular myocardium; *16*, mural cusp; *17*, anterolateral commissure. D, This section is cut at a point near the posteromedial commissure and passes through the coronary sinus. *18*, Posterior wall of left atrium; *19*, coronary sinus; *20*, terminal portion of the circumflex coronary artery; *21*, posteromedial commissure. An encircling suture would lie in the vicinity of the point indicated by the lines marked *S*.

ventricular region was studied and several methods of placement of the suture were considered.

Discussion of the anatomy of the mitral ring can be simplified by arbitrarily dividing this quasicircular structure into three zones of its circumference (Fig. 2). The most important of these is the medial zone in which the ring is in intimate relationship with the left coronary artery, the aorta and aortic valve, the base of the interatrial septum, the top of the interventricular septum, the tricuspid valve ring, and the coronary sinus. In the anterolateral zone the ring is in anatomic relationship with the proximal portion of the circumflex coronary artery and with the terminal portion of the great cardiac vein. In the posterolateral zone the terminal branches of the circumflex coronary and the proximal portion of the great cardiac vein and coronary sinus are the important associated structures. By cutting off the left atrium as near the annulus fibrosus as possible (Figs. 2 and 5), as well as by sectioning the ring radially at various points (Figs. 3 and 4) one can readily demonstrate a periannular space, occupied by epicardial fat and loose connective tissue, which courses around the ring throughout its circumference. In the anterolateral and posterolateral zones this space separates the vascular structures from the valve ring proper and thus facilitates the placement of a circumannular suture without injury to these vessels. Furthermore, both the circumflex coronary artery and the great cardiac vein, in their encircling course, tend to spiral gently away from the ring and all of their significant branches are directed centrifugally and, therefore, do not interfere with the intended instrumentation. By examining the radial sections of the ring the boundaries of the periannular space at various points can be demonstrated. A section at a point adjacent to the aorta shows the narrowed space bounded inferiorly by the fusion of the aortic and mitral valve rings, internally by the left atrial wall near the base of the appendage, and externally by the aortic wall forming the posterior sinus of Valsalva. A section at the junction of the medial and anterolateral zones reveals the external boundaries to be the encircling vessels

and their coat of fat and pericardium, inferiorly is the rim of the left ventricular myocardium, internally is the insertion of the left atrial wall, forming the base of the atrial appendage on the annulus at a point near the anterolateral commissure. Sections at the junctions of the anterolateral and posterolateral zones and the posterolateral and medial zones show similar demarcations. In the latter section, however, the great cardiac vein has become the coronary sinus, and the circumflex coronary has either turned downward out of the way or has ramified into insignificant filaments. A cut at a point near the posteromedial commissure passes through the base of the interatrial septum and cuts the rings of the tricuspid, as well as of the mitral valves. Further down it sections the top of the interventricular septum. Here the periannular space is smallest and is bounded inferiorly by the interventricular septal rim and on either side by the rings of the atrioventricular valves and the insertions of the interatrial septal walls into the corresponding fibrous rings. In the intact fresh heart a blunt probe, bent to conform to the curvature of the ring, can be guided by an intra-atrial palpating finger to pass within the space from anterior to posterior, entering at a point about 1 centimeter from the origin of the circumflex coronary, passing either beneath or over it, and emerging either above or below the coronary sinus posteriorly, at a point 1 or 2 centimeters from the junction of the sinus with the right atrium. Passage of the probe around the other two zones of the ring presents no difficulty. Certain risks are inherent in the maneuver of threading a suture around the medial zone in a beating heart. These include the danger of puncturing the sinus of Valsalva, or of transfixing a segment of aortic or mitral valve cusp, as well as the possibility of penetrating endocardium at two opposite points, leaving a "cord" of suture within the chamber which could cut through the atrial wall or could serve as a nidus for thrombosis. There are several ways of avoiding these pitfalls and at present investigation of a number of methods for placement of the suture to establish the safest and simplest technique is being undertaken.

Fig. 5. A view into the left atrioventricular ring with the left atrium removed. Same view as Figure 1. The probe passes beneath the circumflex coronary artery (arrow on left) and enters the grooved floor of the transverse sinus before penetrating the interatrial septal segment. The arrow which is shown on the right indicates the course of the coronary sinus.

The scope of this paper is limited to the introduction of the rationale for this approach to the surgical treatment of mitral insufficiency and to the presentation of the anatomic features which make the method feasible. In the course of our future studies we are also endeavoring to determine the best suture material to be used, as well as to establish to what extent surgical trauma and cicatricial changes may affect the intended purpose of the procedure.

SUMMARY

1. A brief discussion of past attempts surgically to correct mitral insufficiency is presented.

2. The rationale of placing a constricting suture to limit or decrease the size of the atrioventricular ring is suggested.

3. The anatomy of the region involved is described, based on a series of dissections on human hearts, and with particular attention to the features which apply to the proposed technique.

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OBSERVATIONS ON THE MECHANISM AND FUNCTION OF A TIDAL DRAINAGE APPARATUS

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THE treatment of neurogenic disorders of the urinary bladder has presented problems which have elicited many techniques of solution. Munro and Hahn (7) developed a fundamental pattern for a tidal drainage apparatus which served to drain the bladder at predictable intervals, permitting control of intravesical pressure as well as intermittent irrigation of the viscus. They arranged for intravesical pressure measurements which could be used in the categorization of the type of bladder injury (6). The original apparatus was subsequently simplified and attention directed to the several patterns of bladder activity as observed on the cystometer.

Further modifications of the original tidal drainage apparatus were made by Bellis, Stewart, Cone and Bridgers, and MacNeill and Bowler. Many of these modifications represented improvements. They all pointed out the soundness of the original principles which Munro recognized in the original apparatus. However, Dr. David Cheever, of Boston, in discussing Munro's original paper expressed the feelings of the medical profession in using this device, when he said: ". . . . I am not a graduate in hydraulic engineering. I don't mind saying that I don't fully understand the apparatus" (6).

This statement, first made in 1935, is still being made in 1953. Some physicians, as Deming has pointed out, have discarded tidal drainage in the treatment of neurogenic bladders because they have been unable to train their resident and nursing staffs in its use.

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At the request of the resident staff of the Seattle Veterans Hospital, the senior author undertook an analysis of the tidal drainage apparatus used at the hospital (Fig. 1). This analysis was made from the point of view of a hydraulics engineer (5), but was influenced by the inherent impulses of his surgical colleagues to improvise and modify.

STATEMENT OF THE PROBLEM

The principle utilized in tidal drainage is that of the hydraulic siphon. The apparatus analyzed is diagrammatically shown in Figure 2. The graduated vessel contains the external supply which is controlled by a screw clamp. Clamp adjustment produces any desired number of drops per minute through the airtight glass cylinder. The solution passes through rubber tubing (hereafter referred to as tube 1) to a glass wye (Y_1) where a vertical glass tube (tube 2) is connected to the system for the purpose of admitting air required to break the siphon and to serve as a cystometer. Flow is then directed through tube 3 to Y_2 and finally to the catheter (tube 4) which passes into the bladder.

Both external and internal (kidney) supplies act to build up enough pressure in the bladder to drive a column of liquid over the inverted U-tube. Siphon action follows and the bladder discharges into the jar on the floor. Thus the elevation of the U-tube dictates the maximum pressure and volume of the bladder, and extreme stretching of the viscus is eliminated.

Siphon action breaks when the column of liquid in tubes 2 and 3 drops to Y_2 thereby permitting introduction of air to the U-tube. Observation of hospital equipment in operation showed that the average time between discharge periods was 30 minutes. This meant that siphon action broke before the bladder

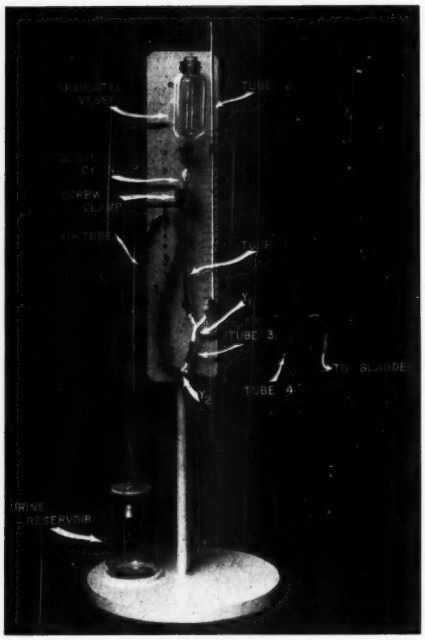

Fig. 1.

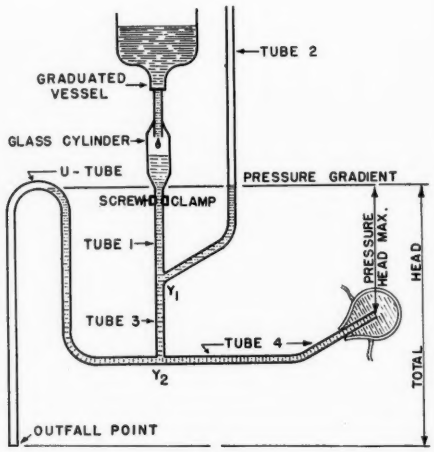

Fig. 2.

Fig. 1. The tidal drainage apparatus used at the Seattle Veterans Administration Hospital. It is diagrammatic in setup, extremely adaptable for all circumstances, and easily constructed at low cost.

Fig. 2. Diagram of the fluid levels in the tidal drainage apparatus just before the siphon action. Note that the bladder is full; the fluid level of tube *2* is the same as that of the U-tube.

was completely drained. The following approximate calculation bears out this reasoning:

Volume of normal bladder when full = 500 c.c.
Average normal time for internal filling = 3 hours

$$\text{Average rate of internal supply} = \frac{500}{3} = 167 \text{ c.c./hr.}$$

Average rate of external supply = 10 drops per min. = 30 c.c./hr.
Considering simultaneous supply,

$$(167)t \text{ plus } (30)t = 500$$
$$(197)t = 500$$
$$t = 2.54 \text{ say } 2\tfrac{1}{2} \text{ hours}$$

Where t = average time required to fill a bladder receiving both internal and external supply.

Since a bladder filled to the siphon point in approximately one-fifth this time, only 100 cubic centimeters must have been contributed. The bladder must have already contained 400 cubic centimeters, hence it was close to 80 per cent full when the previous siphon broke. The problem then was to prolong the siphon until the bladder was empty, thereby creating a condition closer to normal within the patient.

LABORATORY APPARATUS

The laboratory apparatus closely resembled that in use clinically with the exception, of course, of the actual human bladder. To simulate the organ a small beach ball was first utilized, but it was soon discarded, being oversized. The bladder of a pig functioned extremely well for a brief time only. Final selection was a toy balloon which held up well and performed satisfactorily in all respects. Figure 3 illustrates the artificial bladder installation. The purpose of the bottle was to provide a maximum allowable volume as would be the condition within a patient. The U-tube was made of glass for viewing facility. All tubing was approximately the same size used clinically, including the smaller catheter tube in line 4. The position of the bladder and the U-tube was adjustable.

LABORATORY PROCEDURE

First efforts were directed toward revision of the system. Since air reached Y_2 too soon, line 2 was blocked, resulting in complete bladder discharge but a continuous siphon.

Next, a double siphon was employed and the apparatus presently developed into a workable but considerably more complicated scheme.

Equipped with a fairly suitable revision, the writers then sought the fault of the original system. It soon became evident that analysis of the old should have preceded design of the new, for improper adjustment was found to be the source of all troubles. Thus, the double siphon arrangement was discarded and is not worthy of further mention since unnecessary complication of an apparatus is certainly not good practice.

ANALYSIS

The reason for the incomplete discharge during a single siphon action and other facts pertinent to proper functioning of the apparatus became clear through construction of the hydraulic gradients at the critical periods throughout a complete cycle of operation. Figure 2 illustrates the condition existing just before the siphon starts. Due to low velocities during the filling process, head losses (energy loss due to friction) can be neglected and the pressure gradient is a horizontal line. Note that tube 2 and the U-tube act as piezometers (or cystometers) registering the pressure heads at Y_1 and Y_2 respectively. Maximum pressure on the bladder occurs just as flow starts over the U-tube.

With the beginning of bladder discharge the gradients shift to those shown in Figure 4. Now tubes 2 and 3 operate as a single piezometer (or cystometer) at the point Y_2. Intake loss, velocity head, and friction loss act to create a rapid drop of pressure head at Y_2, accounting for the abrupt fall of the column in tubes 2 and 3. Line 1 now remains full to the point Y_1, continuing to discharge approximately 10 drops per minute into tube 3, then directly out of the system.

Volume decrease of the bladder during the discharge is accompanied by pressure drop at that point. Therefore, the total head (from bladder to end of U-tube) is diminished. This continues until zero pressure head occurs at Y_2, since the admittance of air then breaks the siphon.

Figure 5 depicts the gradients just as the siphon is about to break. Note that positive pressure still exists at the bladder, indicating the bladder has not yet completely emptied.

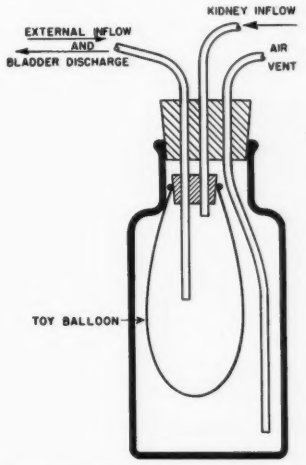

Fig. 3. The artificial bladder used in the analysis of the tidal drainage apparatus.

Following the siphon break, tubes 1 and 4 remain full, as in Figure 6, and a new cycle begins with the bladder filling. Contribution from both external and internal supplies causes gradual filling of tubes 3 and 2 and the U-tube until the condition of Figure 2 is again reached.

Apparently then, proper functioning of the apparatus depends upon the elevation of Y_2. This point becomes a key adjustment, its ideal position being that which will insure atmospheric pressure simultaneously with an empty bladder. Figure 7 shows the key adjustment. The dashed portion of the sketch reproduces Figure 5 to amplify the attunement.

Experiment confirmed the theory. Y_2 was varied in elevation by increments of about 3 inches and each lowering resulted in an increased volume of discharge for a single siphon action. Most favorable position to produce an empty bladder was readily found by trial adjustment.

The ideal position of Y_2 actually represents a minimum elevation above outfall, since further lowering would result in a positive pressure at the point when bladder volume is depleted. Thus the siphon would never break and the bladder would not fill.

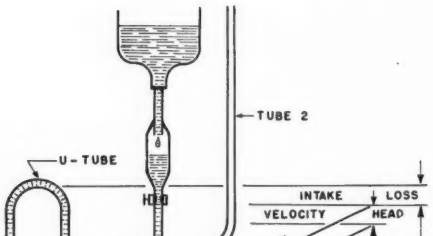

Fig. 4. The siphon has commenced to empty the bladder. Air already has filled tube 2 and is entering tube 3. It lacks but a short distance to enter Y_2 and thus break the siphon.

Y_2 must lie between the elevations of the bladder and the outfall point. Best positioning in practice should be determined by the following steps:

1. Induce the first siphon action with Y_2 at or below the elevation of the outfall point. This insures a continuous siphon. Indication of an empty bladder will be when the discharge reduces to a trickle (the external supply only).

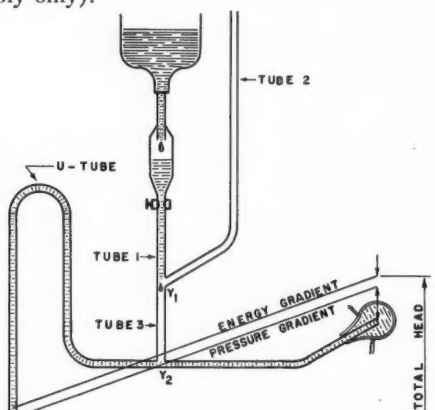

Fig. 5. Air is now about to enter the U-tube line through Y_2. The bladder has been emptied of all but a small amount of urine.

2. When the bladder has emptied, raise Y_2 until the siphon breaks. Now the limits of the adjustment are defined and the system is ready for a new cycle.

3. Lower Y_2 to 1 or 2 inches above the original setting. If the siphon does not break at completion of the next discharge, repeat step 2 and set Y_2 once again a short distance above the previous elevation.

Adjustment should take no longer than 2 cycles and each cycle can be accelerated by increasing the external supply to maximum during filling. On familiarizing himself with the apparatus an operator will find the adjustment a simple operation.

Another consideration has possibly already become apparent to the reader. Adjustment can also be carried out by making Y_2 a fixed point and regulating the elevation of the outfall point. While this would be a simpler operation, it is not recommended because breaking of the siphon is more pronounced with a high velocity through the system. Therefore, difference in elevation between patient and outfall point should be kept a maximum. Economy consideration also favors setting of a maximum total head. Since the solution used for external supply is wasted during the siphon period, discharge should be rapid.

The outfall point should not be submerged in the receiving container since the rise of surface elevation in the filling bottle would then create back pressures affecting the ideal positioning of Y_2. Receiving bottles should be stoppered with corks having 2 holes, one to receive the end of the siphon tube, the other allowing air escapement.

POSSIBLE REVISIONS

When the siphon action breaks, all of the fluid beyond Y_2 flushes from the system, but tube 4 remains filled with waste solution from the bladder (see Fig. 6). If, at this stage, external supply exceeds that of the kidney function, the fluid in the catheter will return to the bladder. This undesirable backing up can be minimized by placing Y_2 as close to the bladder as possible. Such a revision, however, precludes adjustment of Y_2 to a critical elevation, necessitating an alternate arrange-

ment. Figure 8 illustrates the improvement and introduces the new adjustment. (Compare Fig. 8 with Fig. 1.)

Tube 3 is lengthened into a U-tube, thereby permitting negative pressures at Y_2 without the admission of air. Column heights in tube 3 are shown for each of the labelled successive gradients during the discharge. Now the critical adjustment becomes the invert of tube 3. If the U-tube is extended below that position shown in the sketch, siphon action will not stop because air will never reach Y_2. Critical position of the tube 3 U-tube to insure complete bladder discharge will be a distance below Y_2 equal to (or slightly less than) the maximum negative pressure head (h), developed at Y_2 when the bladder is empty. When the U-tube column has dropped to the invert, it is immediately drawn into the main flow line with further drop in pressure at Y_2.

Instructions for the U-tube adjustment would parallel those already presented with the exception that the wye remains fixed, and the U-tube elevation is varied. This revision is most satisfactory from patients' point of view, and has less chance for human error than following revisions.

Another refinement is illustrated in Figure 8. Y_1 is raised to an elevation above the crown of the siphon tube to insure closer control of the external supply. (Refer to Fig. 6.) Following the siphon break the pressure at Y_1 is atmospheric; therefore, the pressure within the glass cylinder is negative by the amount $\frac{(x)(62.5)}{144}$ psi. When filling drives a column into tube 2 a back pressure develops at the cylinder, thus the rate of external supply decreases. In fact, if the reservoir is below the crown of the siphon tube, external flow will stop when the column in tube 2 reaches the reservoir surface. By extending tube 3 so that the rising column will never reach Y_1, pressure within the glass cylinder remains constant and the number of drops per minute become a function of only the static head (z). This distance can be kept relatively constant for a large number of cycles through utilization of a larger reservoir. Accurate control of the drops can be realized with one pinch clamp adjustment and maintenance of a fairly constant reservoir level on the part of the operator.

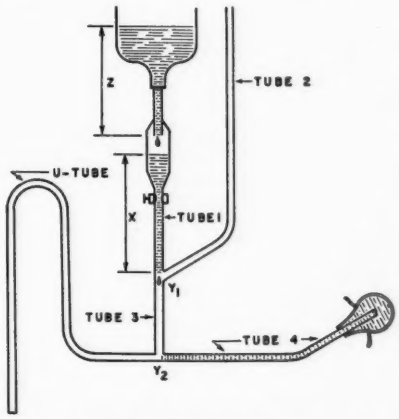

Fig. 6. Air has now entered Y_2 and displaced the fluid in the ascending limb of the U-tube, thereby breaking the siphon. The cycle may now start again with the filling of the bladder from the kidneys and the reservoir. Note that during the emptying cycle there has been a continuous drip of fluid from the reservoir, although it was wasted by going out through the U-tube.

Still another possible adjustment to prolong the period of siphon action is that suggested

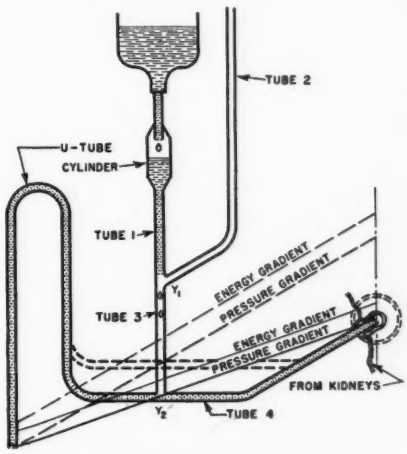

Fig. 7. This diagram shows how the adjustment of the level of Y_2 is critical in the complete emptying of the bladder. With Y_2 lowered so that air intake is delayed, complete emptying of the bladder can be achieved.

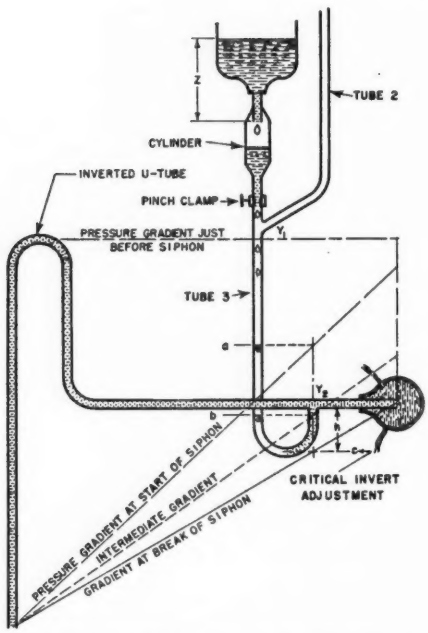

Fig. 8. One possible revision of the apparatus would include the elevation of Y_1 above the level of the siphon. Tube 3 and the U-tube would then have to act as the cystometers. (This is essentially the arrangement preferred by Cone and Bridgers.) The incorporation of a second U-tube at Y_2 will serve to minimize reflex of fluid from the catheter during filling.

by Cone and Bridgers. The narrowing of the air inlet of tube 2 by the addition of a capillary tip to the top will serve to delay the entry of air into Y_2 until the siphon has been active for long enough to empty the bladder. This adjustment is less adaptable than the changes in the level of Y_2 or the tube 3 invert and it is not acceptable from a hydraulic point of view, because of the fact that it acts to hamper normal hydraulic performance of the system.

Finally, the cystometer can be combined with tube 3, as per Cone and Bridgers, and the air break achieved by a small opening in the Murphy drip cylinder. This gives greater simplicity of function. Tube 1 would then have to be made of glass and the Murphy drip would have to be above the crown of the siphon tube.

SUMMARY

In summary, all considerations requisite to the proper setup of the apparatus should now be stated.

Elevation of the patient can be fixed by the height of the bed. The outfall point should be fitted into an air-free cork in the receiving container placed on the floor. The siphon U-tube should be fixed a vertical distance above the bladder which will develop the maximum pressure (therefore volume) most suitable to the particular patient. Complete discharge depends upon the elevation of Y_2, or the invert of the U-tube connected to Y_2, depending upon the apparatus used. Adjustment to the critical elevation should follow in order with the steps previously given. Set Y_1 2 or 3 inches above the siphon U-tube to insure the impossibility of developing back pressures at the glass cylinder. Elevations of the cylinder and the reservoir are immaterial, since the pinch clamp adjustment controls the external quantity.

Before connecting the apparatus with the catheter, the pinch clamp is opened until all air in the tubes is displaced by solution. Hence, no air will be available for passage into the bladder.

CONCLUSION

The tidal drainage apparatus, as devised by Munro and subsequently modified by others, has been examined from a hydraulic viewpoint. The theory is based on the hydraulic siphon, influenced by filling from an external source (the irrigator) and an internal source (the bladder). The set off of the siphon is produced and affected by the combined action of both of these sources and is controlled by breaking of the siphon with air at the proper moment of bladder emptying. A variety of adjustments are possible with this device, depending upon the clinical problem which is involved as well as the point of view of the physician.

A semidiagrammatic apparatus has been devised to permit these many adjustments. This apparatus has been proved practical in its application to patients and is suggested as a means of teaching others to understand tidal drainage better.

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THE COMMON CHANNEL FOR BILE AND PANCREATIC DUCTS

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STUDIES of the common bile duct have indicated that anatomic variation exists in blood vessels, lymphatics, nerves, and surrounding tissues. However, more complete investigations have shown that the anatomic course and characteristics of the common bile duct are standard and uniform with few variations.

Many authors use inadequate terminology in referring to the common bile duct and its termination. For example, the termination of the common bile duct is known to be comprised of several groups of sphincter muscles which surround the termination of the common bile duct. Yet, this muscular portion of the duct is designated as an "ampulla." Etymologically speaking, a papilla designates a "mass," while an ampulla indicates a "space" or dilation.

Previous investigations have confirmed the anatomic "papilla" but have not identified an "ampulla."

It was proposed to determine whether there was an "ampulla," and to ascertain the nature of the common channel for the common bile and pancreatic ducts.

Cadaver and autopsy specimens were obtained. The pancreatic and common bile ducts were injected with pigmented, radio-opaque gels. The specimens were cleared to transparency thus permitting examination in the intact specimen. Autopsy material was also studied with reference to clinical history and general findings.

METHODS OF PROCEDURES

Specimens included the common bile duct from its junction with the cystic duct through its termination. In cadaver specimens, the duodenum and pancreas within 4 centimeters of the termination of the common bile duct were procured. In some cases, the ducts, their termination, and the immediately adjacent tissues only were removed. This was done when the tissues were firm and not autolyzed. In fresh autopsy material, the duodenum and adjacent pancreas were removed en masse, and the specimens placed in a "deep-freeze" for 1 to 3 days. Specimens were studied after additional dissection and were then placed in 4 per cent formalin solution for at least 1 week.

Solutions used for injection into the ducts were colored by the addition of lead chromate (25 gm.) and mercuric oxide (25 gm.) to 15 cubic centimeters of solvent. This solvent was prepared by mixing gelatin (10 gm.) and sodium iodide (10 gm.) with 100 cubic centimeters of distilled water on a water bath. One drop of aerosol was added to accelerate the mixture.

The red-pigmented, lead-containing, gelatin-iodide fluid was injected into the pancreatic duct. The yellow, mercury-containing, gelatin-iodide fluid was used for injection into the common bile duct. A cotton pledget saturated with collodion was placed over the dry tip of the papilla. The dyes were injected after intubation of the ducts with corresponding sizes of polythene catheters. The specimen was then replaced in 4 per cent formalin solution to permit hardening of the colloidal (gelatin-iodide) material in situ. After 3 to 5 weeks, 61 of the 100 formalinized specimens were bleached in sodium hydroxide solution for 3 to 4 days. The specimens were dehydrated and then passed through increasing concentrations of methyl salicylate in order to "clear" the tissues. The specimens were kept in methyl salicylate for further study.

Black and white, color, and infrared photographs, and stereoscopic roentgenograms were taken of most of the specimens. Measure-

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ments were made and all specimens examined under the dissecting microscope.

ANATOMIC FINDINGS

Sufficient control specimens were available in addition to the hundreds of specimens examined previously to give a clear picture of the termination for the common bile duct (Table I). General observations on the terminal portions of the common bile and pancreatic ducts confirmed my previous reports (6, 7).

In this series, the average diameter of the duct was found to be 0.56 centimeter. It was observed that a duct lumen greater than 1.0 centimeter in diameter was abnormal. Abnormalities in size of the common bile duct were found secondary to contained calculi and the presence of benign and malignant tumor. No correlation was observed between variations in the extraduodenal common bile duct and the normal characteristics of the duct termination. The length of the papilla averaged 1.47 centimeters. The diameter of the wall of the papilla averaged 0.69 centimeter (Table I).

The length of the common bile duct in its transpapillary course averaged 1.26 centimeters. This was longer than the pancreatic duct (0.89 cm.).

Sixty-one specimens were prepared by the injection of dyes and cleared to transparency. Separate orifices for both common and pancreatic ducts were observed in 23. In 2 specimens, only the common bile duct traversed the papilla of Vater. In these cases, the pancreatic duct was atrophied and the pancreas emptied through the accessory pancreatic duct. Thus, in 25 specimens there was no possible intermingling of pancreatic and biliary tracts.

In the entire group (100 specimens) the termination for the common duct was observed in four normal categorical types:

(1) Completely separate orifices—42 per cent (Fig. 1); (2) common channel starting in distal third of the papilla—38 per cent (Fig. 2); (3) common channel starting in middle third of the papilla—14 per cent (Fig. 3); common channel starting at proximal third of the papilla—3 per cent (Fig. 4).

TABLE I.—AVERAGE MEASUREMENTS OF 59 SPECIMENS

		cm.
1.	Diameter of extraduodenal common bile duct...	0.56
2.	Length of papilla.....	1.47
3.	Greatest thickness of wall of papilla.....	0.69
4.	Length of transpapillary common bile duct.....	1.26
5.	Length of transpapillar pancreatic duct.....	0.89
6.	(a) Length of common channel (36 cases).....	0.4
	(b) Length of papilla when common channel was present.....	1.6
7.	Diameter—orifice of the common bile duct.....	0.12
8.	Diameter—orifice of the pancreatic duct.....	0.09
9.	Diameter—orifice of the common channel for the common bile and pancreatic ducts.....	0.1

In 60 per cent of cleared specimens the common bile and pancreatic ducts merged. This common channel varied from 0.1 to 1.2 centimeters in length. However, in these specimens the average length of the common channel was 0.4 centimeter, as compared to the average length of the papilla of 1.6 centimeters.

It was found that in 75 per cent the common channel traversed only the distal third of the papilla. In 22 per cent the common channel was in the distal two-thirds of the papilla. In only 3 per cent did the common channel occupy more than two-thirds of the papilla. These results confirm previous findings of the space relations of the common channel to the papilla (6, 7).

There were minimal variations in the diameters of the ducts in those instances in which a common channel existed. The diameters of the ducts' orifices ranged from 0.05 centimeter to 0.4 centimeter. The smallest average diameter in the pancreatic duct was 0.01 centimeter. The common bile duct average orifice was 0.13 centimeter. The average

TABLE II.—SUMMARY OF SPECIMENS

	X-ray studies	Dissections	Totals	
Two orifices.....	19	23	42	80
Common channel less than ⅓ length of papilla.....	11	27	38	
Common channel less than ⅔ length of papilla.....	6	8	14	
Common channel more than ⅔ length of papilla.....	2	1	3	
Not identified.....	1*	2*	3*	
Total.....	39	61	100	

*Only one orifice identified: pancreatic duct not seen through papilla (Cf. text)

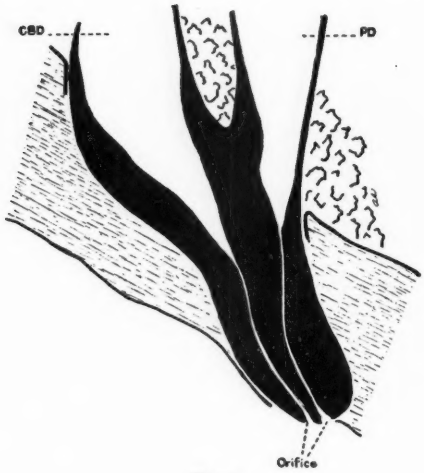

Fig. 1.

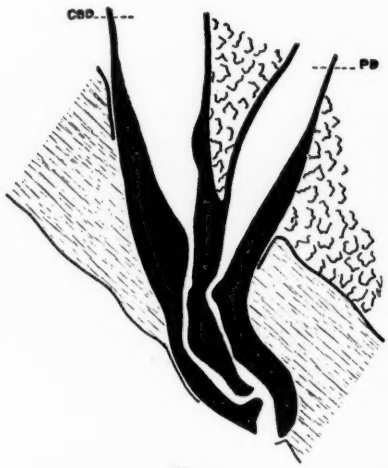

Fig. 2.

Figs. 1, 2, 3, and 4. Line drawings of the transparent injected specimens of the papilla of Vater. The common bile (left) and pancreatic (right) ducts are illustrated in their courses through the papilla and in relation to the duodenal wall in the four normal types of ducts' terminations. CBD, common bile duct; PD, pancreatic; CC, common channel; lined area, duodenal wall; curved line area, pancreas; cross-hatched area, papilla (sphincter muscles).

Fig. 1. Specimen 11—42 per cent. The length of the papilla was 0.8 centimeter. The papilla had two separate orifices. Sphincter tissue was uniformly distributed around both pancreatic and common bile ducts, decreasing at the termination of the ducts. In the proximal third of papilla, common bile duct lumen narrowed abruptly in diameter.

Fig. 2. Specimen 21—38 per cent. The length of the papilla was 1.5 centimeters. There was a single orifice. The papillary muscle tissue was well developed. The ducts' diameters rapidly decreased. The ducts were parallel through at least two-thirds of the transpapillary courses. The axis of both pancreatic and common bile ducts was that of a flat S-shaped curve with many tiny irregularities. There was more interductal than circumductal muscle. At about the junction of middle and distal thirds of the papilla, the common bile duct made a sharp right-angle turn to enter with the pancreatic duct into a shallow common channel. The specimens which are included in this group had common channels which ranged from 0.1 to 0.6 centimeter in length.

diameter of the orifice for the common channel was found to be 0.17 centimeter.

It was found to be just as common for a slight dilatation to occur in the course of the common bile or pancreatic ducts as in the route of the common channel. These segments of dilatation were slight compared to the length and breadth of the papilla and its contained ducts. An ampulla was seen in only 2 cases of this entire series.

In 42 per cent of all cases, separate channels were present for the common bile and pancreatic ducts. This might imply that in the remaining 58 per cent of specimens a common channel existed which would permit interductal reflux. This thought was not confirmed. Careful examination was made of the sphincter muscles with relation to the ducts. It was seen that a common channel which traversed more than two-thirds of the papilla was the only type which could permit interductal reflux.

Analysis, therefore, revealed that only in 3 per cent of the cases could such reflux occur normally between common bile and pancreatic ducts. In an additional 14 per cent a functioning common channel might permit interductal reflux.

DISCUSSION

Job, in 1922, found that 95 per cent of specimens had separate orifices while Opie, in 1903, found only 11 per cent. The average findings in 1,252 specimens (6) indicated that 30 per cent have separate orifices for the pancreatic and common bile ducts. Variations in this group in regard to the incidence of common channel were from 11 to 80 per cent.

Review of the figures reported by previous observers demonstrates a common denomina-

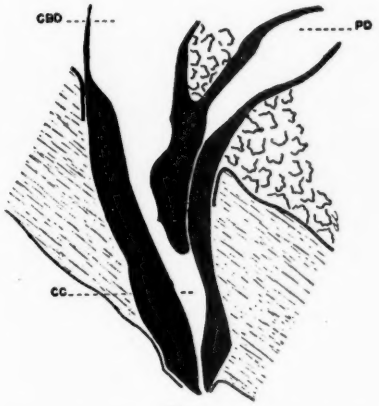

Fig. 3.

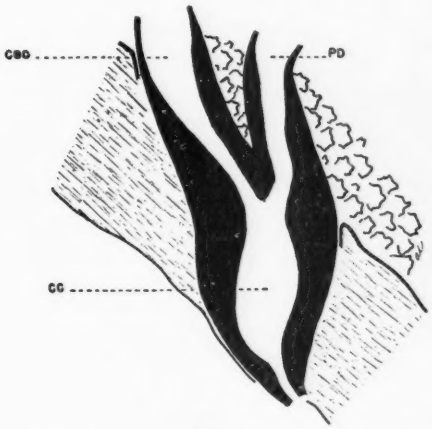

Fig. 4.

Fig. 3. Specimen S-4—14 per cent. The length of the papilla was 0.8 centimeter. There was a single orifice at its apex. At the entrance of pancreatic and common bile ducts into the papilla, their lumens decreased. Toward the middle of the papilla, the ducts merged and there was a widening in the diameter of the common channel. This slight dilatation resembled the concept of the "ampulla."

Fig. 4. Specimen 3—3 per cent. A common channel for pancreatic and common bile ducts traversed more than half of the papilla. The papilla was conical and firm with a single orifice. There was a well developed muscular structure in the proximal half of the papilla. There was a gradual decrease in the diameter of the common bile duct as it traversed the proximal portion of the papilla. The pancreatic duct, however, decreased rather abruptly in diameter. The pancreatic duct joined the common bile duct at the junction of the proximal and middle thirds of the papilla to form a common channel for 0.9 centimeter.

tor. If the depth of the duodenal mucosa was less than 3 millimeters, slight tension on the mucosa would evert the "cupped" lips overlying the papillary orifices. In addition, a redundancy of about 3 millimeters would form a mucosal well around the ducts' orifices. Reevaluating these reports, it is seen that in Reinhoff's series there are 61 per cent and in Mann's studies there are 76 per cent of cases in which separate orifices could have existed. Similarly in the work of Dardinski there are 68 per cent of cases with separate orifices at a distance of 2 millimeters.

This relative distance is very important in determining the existence of a common channel. In 18 cases of 50 (36 per cent) which I dissected (6) a common channel was found for the common bile and pancreatic ducts. In the group, the length of the common channel varied from 1.2 to 8.4 millimeters, averaging 4.4 millimeters. This must be compared to the relative length of the papilla of 14.4 millimeters. In all, the papilla was usually approximately 1 centimeter longer than the common channel.

In the investigations reported herein on untraumatized transparent specimens with a common channel, it was found that in 70 per cent the common channel was in the distal third of the papilla. It was found that in 25 per cent the common channel traversed the distal two-thirds of the papilla.

It is of significance that even in the presence of a "common channel" there is a sturdy disposition of strong sphincter muscle proximally. This is further elucidated by cross-sections (6).

Because of the narrow caliber of the duct termination and its thick muscular wall at the sphincter of Oddi the stone at the terminus of the common bile duct meets an impasse. The stone smaller than 3 millimeters may pass. Under varying circumstances the stone can (a) become impacted, (b) penetrate into the duodenum, or (c) pass through into the pancreas.

The gallstone, if it passes the sphincter muscle, can be dislodged easily into the duodenum. The presence of a stone at the termination of the common duct will not in itself

permit interductal reflux. However, the formation of a diverticulum, fistula, or false "common channel" may be initiated by a calculus moving from the common duct's lumen by erosion into the pancreatic duct. This can produce an abnormal route for interductal reflux. This type is not related to the normal structure of the papilla or the usual routes for the contained ducts.

SUMMARY

1. The termination of the common bile duct (a) is transduodenal, (b) is at a papilla, (c) has a lumen which decreases in diameter like a funnel, (d) curves through a three-dimensional route frequently intertwining with the pancreatic duct, (e) unites with the pancreatic duct to form an anatomic common channel in 55 to 60 per cent of cases.

2. A common channel for the bile and pancreatic ducts which is less than one-half of the transduodenal portion of the common bile duct does not readily permit interductal reflux because of the anatomic disposition of the sphincter.

3. A functioning common channel to permit interductal reflux may exist in 15 per cent of cases.

4. An anatomic common channel for the common bile and pancreatic ducts is not synonymous with, nor should it be confused with the phenomenon of interductal "reflux."

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SELECTIVE SURGERY FOR PEPTIC ULCER

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THOUGH gastrectomies are being performed in ever increasing numbers the world over for peptic ulcer, we have for long felt a new step forward to be due in the surgery of this disease. Gastroenterostomy and limited gastrectomy have failed to control the tendency to relapse in many cases; on the other hand, the very radical gastric resections now widely practiced, though they are rarely followed by ulcer recurrence, have brought with them a number of undesirable side effects which have marred too many of the clinical results.

The problems of duodenal and gastric ulcer are quite different ones, for whereas the former is characterized by hypersecretion of hydrochloric acid and carries a relatively high recurrence rate after limited gastric resection, the latter is associated with a low level of acid secretion and is seldom followed by anastomotic ulcer after gastrectomy. We have, therefore, deplored the use of more and more radical resections in cases of gastric as well as of duodenal ulcer and it has been our endeavor always to conserve as much healthy gastric wall as possible in all patients with plainly benign ulcers of the stomach. Since it is not possible to be absolutely sure of the simple nature of any gastric ulcer at laparotomy, it has been contended that all gastric ulcers should be resected as radically as though definitely malignant. It must be added in vindication of our practice, therefore, that not a single patient of the 180 operated upon for gastric ulcers considered benign at laparotomy has subsequently developed evidence of gastric cancer. On the other hand, 6 patients thought to have carcinomatous ulcers at laparotomy were subjected to radical resections, but their ulcers proved benign at microscopy and 2 of these patients figure among our poor results.

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Eight years ago, stimulated by the work of Dragstedt, we set out to discover whether vagotomy would prove an adequate operation for duodenal ulcer as seen in Britain, though we never considered it a suitable treatment for gastric ulcer. At first we used vagotomy alone, employing an abdominal, perhiatal approach (12). We soon found it necessary to add some bypass procedure in most cases and it was not long before we abandoned vagotomy alone altogether for duodenal ulcer and severely limited our use of vagotomy plus gastroenterostomy. However, we have continued to follow up the patients submitted to these operations.

Of the 108 patients who had vagotomy alone from 5 to 8 years ago, just under 60 per cent have received lasting benefit and have led normal lives free from restraint ever since, though only 33 per cent are altogether symptom-free. However, 25 per cent have had to be advised to undergo further surgery and the remaining 15 per cent, though a little improved and not justifying a second operation, still have to have medical care from time to time.

All of the 108 patients survived their operations, including the further surgery mentioned, and 81 per cent now consider themselves in good health and are well satisfied with their results. The majority of the others have but minor complaints. It may be argued that to use the safe though less dependable operation of vagotomy in the first place and reserve the more radical and more dangerous gastric resection for the failures is good honest surgery. We were not satisfied, however, that we should continue to advise patients to undergo an operation, however safe, which could afford them no better chance of permanent relief than 60 per cent.

During this period of study, however, these things had become apparent: (a) Hypersecretion of hydrochloric acid is checked by vagotomy (12). When the nerve section has been

TABLE I.—POLICY SERIES, OPERATIONS SELECTED IN 823 CASES

Type of operation	Duodenal ulcers or duodenal + gastric ulcers	Gastric ulcers	Gastrojejunal ulcers	Totals	Deaths
Polya gastrectomy	206	57	10	273	6
Billroth I gastrectomy	25	110	—	135	0
Polya + vagotomy	299	9	12	320	6
Billroth I + vagotomy	25	8	—	33	0
Gastroenterostomy + vagotomy	30	—	—	30	0
Vagotomy after earlier gastroenterostomy	—	—	14	14	0
Vagotomy after gastrectomy	—	—	18	18	0
Totals	585	184	54	823	
Deaths	11	1	0		12

complete there has been no sign of return to previous levels of acid secretion even after 8 years (8). (b) The course of ulcer disease is profoundly modified by vagotomy. (c) Clinical failures are chiefly caused by the effects of scarring, duodenal obstruction, and gastric retention. As predicted by one of us (4), this gastric retention has also resulted in several instances of gastric ulcer. (d) Though gastric ulcers have occasionally followed vagal resection, recurrent duodenal ulcers are uncommon. (e) The unpleasant side effects of vagotomy, such as diarrhea and malodorous belching, tend to clear up in the course of weeks or months. In a few bad cases they have persisted for a year or two, and our most stubborn case of recurrent diarrhea lasted 3 years. (f) All symptoms regarded as side effects of vagotomy are much less frequent after combined operations (13).

Both we and others have found vagotomy to be successful for gastrojejunal ulcers after earlier inadequate gastrectomy, and we believed, therefore, that it might prevent them if added to such limited gastrectomies in the first place. By using a combination of vagotomy and two-thirds gastrectomy, we hoped to achieve as effective prevention of ulcer recurrence as is gained by radical five-sixths to seven-eighths resection alone, and at the same time win symptomatic results such as go with limited gastrectomy.

The investigation of the American Gastroenterological Association (9) showed that the addition of vagotomy to gastrectomy was not detrimental, the figures being in fact slightly in favor of the combined operation. Since the recurrence rate with radical gastrectomy alone was almost negligible, it was concluded by Jordon that nothing was to be gained by adding vagotomy. Our purpose, however, in dividing the vagi as well, was to make practicable the use of a more conservative gastric resection.

Since, as stated by Reinhoff, even hemigastrectomy alone was followed by only some 10 or 12 per cent of ulcer recurrences, we did not consider it necessary to add vagotomy to our two-thirds resection in all cases, even of duodenal ulcer. We attempted to select those more liable to recurrence without it on the basis of secretion investigations and resected the vagi whenever the bulked 12 hour gastric night secretion aspirated by continuous suction contained more than 20 milliequivalents of hydrochloric acid. Since a small volume of aspirate can so easily be a spurious record of secretion rate, we also accepted more than 45 units of free hydrochloric acid or over 65 units of total acid in the bulked juice as adequate evidence of hypersecretion (6, 8).

The application of this rule led to the use of vagotomy as well as gastrectomy in 56 per cent of our duodenal ulcer patients, but for only 5 per cent of gastric ulcers, and these 5 per cent were many of them juxtapyloric ones (Table I).

Our patients who earlier had had vagotomies combined with gastroenterostomies have with 1 exception continued to have satisfactory results. Their numbers were too small to supply any weighty evidence as to the long term value of this operation, but we have felt that Crile's figures of about 7 per cent recurrence, but under 0.5 per cent mortality, fully justified the continued use of this operation in specially hazardous cases. Since we instituted our present policy, we have reserved vagotomy plus gastroenterostomy for duodenal ulcer patients in whom, on account of obesity and emphysema, or old age, for example, gastrectomy might have been unduly dangerous. *Better a live patient with recurrence than a dead one without.*

Vagotomy alone has continued to be useful for patients with anastomotic ulcers after earlier gastrectomy, for the operative mortality of a second gastric resection is high and the further recurrence of ulcer after it is discouragingly frequent. Vagotomy was occasionally used, too, for recurrent ulcers which had followed gastroenterostomy when the ulcer was small, there had been no hemorrhage, the stoma was unobstructed and well placed, and when there was no adhesion to the colon, if the patient was elderly or a bad surgical risk.

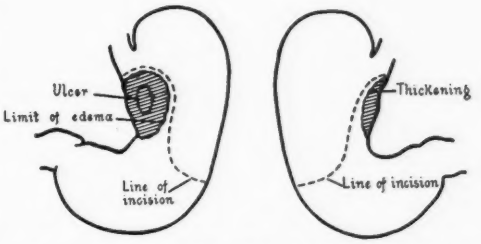

Fig. 1. Diagram showing line of incision when gastric ulcer is high on anterior wall.

TECHNIQUE

Our technique for resection of the vagus nerves has been described elsewhere (5, 7, 11). When vagotomy is to be combined with gastrectomy, it is usual to do the vagal resection first in order that there shall be no risk of introduction of contamination into the mediastinum after the bowel has been opened. It is well to bear in mind that after vagotomy the esophagus is easily stretched and unnecessarily vigorous mobilization can bring the cardia an inch or more down into the abdomen with the result that a surgeon who is not on his guard may easily find that he has resected a greater proportion of the stomach than he had intended. This might even be the reason why some have observed small stomach syndromes more often after gastrectomy plus vagotomy than after gastrectomy alone.

It has recently been the practice of one of us (H. D. J.) to find the midpoints of lesser and greater curvatures with the aid of a few inches of lead wire, and to mark these points with colored sutures before any mobilization of the stomach is undertaken. Since never less than half the stomach is removed, these two sutures are always found on the specimen and the pathologist is then able to deduce fairly accurately what proportion of the stomach has been resected, a valuable record for future reference is then available.

We now regard the Billroth I method of anastomosis after gastric resection, with reestablishment of gastroduodenal continuity, as the operation of choice for patients with gastric ulcers. We used it but little in the past, but in recent years, after observing the satisfactory results which we achieved with it, we have come to employ this method whenever possible. We no longer believe it wise to attempt Billroth I gastrectomy when the duodenal wall is the site of ulceration or scarring. Two patients in whom we had used Billroth I resections for duodenal ulcer were not relieved of their symptoms until a Polya anastomosis had been substituted at a second operation. When a gastric ulcer has been particularly high in position, we have divided the stomach with scissors in such a fashion that though all unhealthy tissue was removed, as much as possible of the stomach was conserved (Fig. 1). This technique has been particularly useful when the ulcer has been high on the anterior or posterior wall.

In the majority of our cases of duodenal ulcer we have performed a Polya gastrectomy resecting about two-thirds of the stomach. The afferent loop of jejunum is taken to the lesser curve and a Hoffmeister spur is made leaving a small stoma, no wider than a dilated jejunum, at the greater curve end, though one of us (H. D. J.) has recently tried a number of left to right anastomoses with the spur still at the lesser curve side in the hope of further hindering the too often precipitate emptying of the gastric stump. We prefer to carry the jejunal loop in front of the colon, where it lies comfortably across the splenic flexure and we aim to make the afferent loop of such a length that there is neither sagging nor dragging. First the gastric remnant is closed, except for the last inch at the greater curve end. Next the stomal anastomosis is made, and, finally, the afferent loop is stitched to the first 1½ inches or so of the reconstituted lesser curve with interrupted sutures. The lie of the loop

TABLE II.—RESULTS IN 892 FOLLOWED PATIENTS (670 POLICY CASES COMPARED WITH 222 ROUTINE RADICAL 4/5 TO 7/8 GASTRECTOMY CASES)

Operation	No. cases	Condition	No. cases	Side effects			Categories			
				Colic	Vomiting or regurgitation of bile	Dumping or hypoglycemic syndromes	1	2	3	4
2/3 Polya gastrectomy	232	DU or DU + GU	174	13%	15%	16%	64%	30%	4%	2.3%
		GU	51	(22%)	(14%)	(18%)	(63%)	(29%)	(8%)	—
		G–JU	7	1 case	3 cases	—	3 cases	4 cases	—	—
2/3 Billroth I gastrectomy	92	DU or DU + GU	17	2 cases	2 cases	5 cases	7 cases	5 cases	4 cases	1 case
		GU	75	(19%)	(12%)	(15%)	(63%)	(35%)	(1.3%)	(1.3%)
2/3 Polya + vagotomy	266	DU or DU + GU	248	21%	15%	24%	58%	38%	3.2%	0.4%
		GU	7	3 cases	3 cases	2 cases	2 cases	4 cases	1 case	—
		G–JU	11	3 cases	2 cases	2 cases	5 cases	6 cases	—	—
2/3 Billroth I gastrectomy + vagotomy	25	DU or DU + GU	17	1 case	1 case	1 case	14 cases	2 cases	—	1 case
		GU	8	1 case	2 cases	—	4 cases	4 cases	—	—
Gastrojej. + vagotomy		DU	30	(13%)	(10%)	(13%)	(54%)	(37%)	(6.7%)	(3.3%)
Vagotomy after G-E.		G–JU	14	2 cases	—	2 cases	11 cases	2 cases	1 case	—
Vagotomy after P.G.		G–JU	11	3 cases	2 cases	2 cases	5 cases	3 cases	2 cases	1 case
Radical 4/5–7/8 Polya gastrectomy	222	DU or DU + GU	138	39%	28%	47%	46%	41%	10%	2.4%
		GU	75	(51%)	(43%)	(49%)	(36%)	(56%)	(7%)	(1.3%)
		G–JU	9	2 cases	2 cases	2 cases	5 cases	4 cases	—	—
All policy ops.		All lesions	670	18%	14%	18%	60%	34%	4.5%	1.5%
Radical gastrectomy		All lesions	222	42%	24%	47%	42%	47%	9%	2.3%

DU, duodenal ulcer; GU, gastric ulcer; G–JU, gastrojejunal ulcer.
In order to discourage comparisons of little statistical significance, percentages are given in parentheses when they are of groups of less than 100. In groups totalling less than 30, numbers of cases are given instead of percentages.
Combined duodenal and gastric ulcers are grouped with duodenal ulcers, for the problem which they present is a similar one.
The fractions 2/3, 4/5, 7/8, refer to the proportions of stomach which it has been aimed to resect.
The third column under side effects gives the proportions of patients who had had attacks of weakness and includes both "dumpers" and those subject to hypoglycemic symptoms, for we found many in whom we could not differentiate these syndromes clinically.

is then tested and another stitch or two added, or one divided, as required.

Mortality. The policy which we have described has now been applied in 823 consecutive cases during the past 6 years and has cost 12 postoperative deaths, a mortality of 1.5 per cent. These were all among patients who had undergone gastrectomy, a mortality of 1.8 per cent for gastrectomy alone and 1.6 per cent for gastrectomy plus vagotomy (Table I). A separate study has been made of deaths following some 3,000 elective gastrectomies from 10 scattered representative hospitals in England during the same period (to be reported later). Among these the average mortality was 4 per cent, being higher where radical resection was in vogue, but similar to our own figure where conservative gastrectomy was the rule.

Comparison of results. During the follow-up of our patients, we have had the good fortune to be invited by several of our colleagues, who have used very radical Polya type gastrectomies routinely for all their cases of peptic ulcer during the same period, to follow their patients along with our own. Only the patients operated upon 12 months or more ago are reported, and of these we have kept trace of 96 per cent and most have been interviewed at regular intervals. During the follow-up period 13 patients died from causes unrelated to peptic ulcer and 4 from unknown causes.

Two of our patients had pulmonary tuberculosis before operation, but are now well. Three patients are known to have developed tuberculosis since operation. Two have recovered, but the third has died.

For the purpose of comparison between groups, patients were asked a number of standard questions to which they could select from two or three possible answers. Though psychologic factors indubitably influenced the patients' self-assessment, it was believed that in the large groups dealt with such factors should balance out and render comparison between groups on the basis of numbers of this or that answer selected, reasonably valid. This method had the virtue that it eliminated the bias of the observer. Questions were not, of course, limited to those on the standard forms, and other complications than those mentioned, such as vitamin deficiency states and anemia, were sought for.

Control of ulcer disease. Two of our patients (0.3 per cent) have developed recurrences of ulceration. One, whose secretion test gave a borderline result, had been subjected to two-thirds gastrectomy alone. He has since been cured by the addition of vagotomy. The other, a gastrojejunal ulcer, followed a gastroenterostomy plus vagotomy. There are 3 other patients (0.4 per cent) who say that their symptoms have not been relieved by their operations and who have continued to complain of pain and vomiting, and 2 now have "dumping" as well.

In the radical gastrectomy group 2 proved recurrent ulcers (1.0 per cent) have developed, and 3 other patients (1.4 per cent) have not been relieved of ulcer-like symptoms.

Side effects and satisfaction with results. It would be futile to pretend that the gastrectomized or vagotomized states are desirable ones. The satisfaction which the patient has with his result is bound to depend largely upon how the side effects in his case compare in unpleasantness with the former symptoms of his peptic ulcer. For this reason the best results are achieved, as in so many surgical operations, in the worst cases.

The commonest of the side effects detected in the follow-up clinic was that of sudden weakness, sleepiness, or giddiness after larger meals, often accompanied by sweating and sometimes by trembling and palpitations. The most frequent description given by patients was that of feeling "done in and useless for about a quarter of an hour after a main meal."

TABLE III.—DUODENAL OR DUODENAL PLUS GASTRIC ULCERS IN 624 CASES

Type of operation	No. cases	Categories, per cent			
		1	2	3	4
2/3 Polya gastrectomies	174	64	30	4	2.3
2/3 Polya gastrectomies + vagotomy	248	58	38	3.2	0.4
2/3 Billroth I gastrectomies	17	7 cases	5 cases	4 cases	1 case
2/3 Billroth I gastrectomies + vagotomy	17	14 cases	2 cases	—	1 case
Gastrojejunostomies + vagotomy	30	(54)	(37)	(6.7)	(3.3)
All policy operations	486	60	34	4.3	1.6
Routine radical 4/5-7/8 Polya gastrectomies	138	46	41	10	2.2

This syndrome occurred from daily to once a month in 18 per cent of the "policy" group and in 47 per cent of the "radical" group.

The next commonest symptom was colic or "wind pain." This was experienced by 14 per cent of the "policy" group, a further 4 per cent having it mildly or infrequently; in the "radical" group 30 per cent had this symptom and a further 12 per cent admitted to mild attacks. Some of these patients in both groups had had colic before operation, too, and said it was no worse.

Vomiting or regurgitation of bile occurred in 10 per cent of the "policy" group and 20 per cent of the "radical" group. A further 4 per cent in each group have rare attacks.

Diarrhea had been a frequent early sequel to vagotomy when we used that operation alone, and 4 per cent of our patients had continued to have intermittent attacks for up to 3 years afterward. Diarrhea is a complication, though less well recognized, of gastrectomy, too, and our figures seem to show that more radical operations are more liable to cause it. There were 5 cases (1.5 per cent) of intermittent diarrhea among the 325 patients subjected to moderate gastrectomy alone and 6 (2.1 per cent) among the 291 followed after vagotomy plus limited gastrectomy. Among the 222 who had had radical gastrectomies, however, there were 10 cases (4.5 per cent).

No vitamin and other deficiency states were observed among the "policy" group, though

TABLE IV.—GASTRIC ULCERS IN 216 CASES

Operation	No. of cases	Categories, per cent			
		1	2	3	4
2/3 Polya gastrectomies	51	63	29	8	—
2/3 Polya gastrectomies + vagotomy	7	2 cases	4 cases	1 case	—
2/3 Billroth I gastrectomies	75	(63)	(35)	(1.3)	(1.3)
2/3 Billroth I gastrectomies + vagotomy	8	4 cases	4 cases	—	—
All policy operations	141	60	35	4	0.7
Routine radical 4/5-7/8 Polya gastrectomies	75	36	56	7	1.3

one or two women patients have required extra iron to maintain normal hemoglobin levels. A few patients with dumping symptoms have restricted their intakes and have failed to gain weight, but these formed a smaller proportion of the "policy" than of the "radical" groups.

All the patients were asked: "Taking everything into consideration, do you find that since your operation you are: (1) normal and apparently cured, (2) a lot better, but not normal, (3) only a little better, or (4) no better at all?" The results have been classified into 4 categories in accordance with the patient's own choice (Table II).

Duodenal ulcer (Table III). Of the 486 patients with duodenal or combined gastric and duodenal ulcers operated upon in accordance with our policy and followed up for more than 1 year, 94 per cent selected one of the top two categories and 6 per cent were failures (only a little better or no better at all). In the routine radical gastrectomy group there were 138 cases of duodenal or combined ulcers. Of these 87 per cent chose categories 1 or 2 and 13 per cent were little or no better or relapsed.

Within the policy group those who had two-thirds Polya gastrectomy without vagotomy appear to have fared slightly better in regard to side effects than those who had vagotomy added, though there were fewer complete failures among the latter. However, it must be remembered that patients who were selected for the addition of vagotomy presented a different problem. It must surely be that a number of them would have developed recurrent ulcers had they been subjected to limited gastrectomy alone.

Very few patients with duodenal ulcers were thought suitable for Billroth I gastrectomies, and deductions from the results must be reserved. However, one cannot but be struck by the difference between those who had had vagotomy as well and those who had not, the former having done much better. We no longer recommend Billroth I gastrectomy for patients with duodenal ulcers.

Though there has so far been only 1 recurrence among the 30 patients who had gastroenterostomy plus vagotomy for duodenal ulcer, we know that other surgeons with a greater experience of this operation have met double this proportion. The operation can be done swiftly and with little risk to life, and herein lies its value for occasional use. When successful the side effects are few.

Gastric ulcer (Table IV). Though we have expressed the view that moderate gastric resection is adequate for the prevention of recurrence after operation for gastric ulcer, there have been cases in which more than two-thirds of the stomach had to be sacrificed owing to the position and size of the lesion. However, our policy has achieved a larger proportion of symptomatically satisfactory results than has that of routine radical resection. Whereas 92 per cent of the latter put themselves in categories 1 or 2 and only 36 in the top group, in the policy series there were 95 per cent in categories 1 or 2 and 60 per cent considered themselves altogether cured and normal.

Among our own series, those who had had Billroth I gastrectomies achieved a higher

TABLE V.—GASTROJEJUNAL ULCERS AFTER GASTROJEJUNOSTOMY IN 41 CASES

Operation	No. of cases	Categories, No. of cases			
		1	2	3	4
2/3 Polya gastrectomies	7	3	4	—	—
2/3 Polya gastrectomies + vagotomy	11	5	6	—	—
Vagotomies	14	11	2	1	—
All policy operations	32	(59 per cent)	(38 per cent)	(3 per cent)	—
Routine radical 4/5-7/8 gastrectomies	9	5	4	—	—

proportion of good results than those who had had Polya type gastrectomies. Though nearly as many had had dumping symptoms at some time, the proportion of those which were mild or infrequent was much greater in the case of Billroth I operation.

Gastrojejunal ulcer (Table V). Operations for anastomotic ulcer carry a higher mortality than those for primary ulcer. In the series of over 3,000 postwar gastrectomies previously referred to, the resections for jejunal ulcer resulted in 16 per cent of deaths. The problem in this condition, therefore, lies less in finding operations which are never followed by further relapse than in reducing the risks of surgery. Though vagotomy alone has cured all of 14 gastrojejunal ulcers after earlier gastroenterostomy for which we have used it, it cannot be dependable for we have had 1 stomal ulcer among 30 duodenal ulcer cases in which vagotomy was added to gastrojejunostomy in the first place. However, it is certainly the least dangerous operation available for jejunal ulcer at present and the symptomatic results in our few patients have been good in most cases.

Eighteen other patients had more advanced lesions which demanded resections and we added vagotomy in 11 of them who had evidence of gross hypersecretion. There were 9 similar cases in the radical gastrectomy group, and though their results are not inferior we believe the routine use of the very high resections to be more dangerous.

A further 11 patients in our own series had vagotomies for gastrojejunal ulcers after earlier gastrectomy. All are cured of their ulcers, but several continue to suffer from the side effects of their operations. Four of the earlier gastrectomies had been very radical ones. Two patients are bad dumpers, 2 have bilious regurgitation, and 3 have attacks of colic. The worst dumper, who put himself in category 4 (no better off for his operation), was recently relieved by a Steinberg jejunoplasty and now puts himself in category 2.

Results for the policy as a whole. In the radical gastrectomy group 42 per cent ranked themselves in category 1 (normal and apparently cured), and 89 per cent put themselves in categories 1 or 2 (a lot better, but not normal). In the policy group 60 per cent chose category 1 and 94 per cent selected one of the top two categories.

Patients were also asked: "Was your operation worth while and, now that you know its effects, if you went back to before your operation, would you have it again"? Of our patients 98.6 per cent replied "Yes," and many used such expressions as "A thousand times, yes," or "Yes, but 20 years sooner."

CONCLUSIONS

Very radical gastrectomy has virtually solved the problem of peptic ulcer recurrences, but the small stomach syndromes which it has brought in its train have to some extent marred the results and have led to the introduction of operations for the restoration of gastric capacity such as that of Steinberg and the more recent ones of Henley and Moroney. Though these are likely to have an important place in surgery for gastric cancer, we have demonstrated how in peptic ulcer cases it is possible both to avoid ulcer recurrence and to conserve gastric capacity at the same time.

Both radical gastrectomy and limited gastrectomy plus vagotomy have been shown to confer a high degree of immunity from ulcer recurrence, but our results have demonstrated that limited gastrectomy with or without vagotomy, as occasion demanded, caused fewer of all side effects and produced the greater proportion of satisfied patients.

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LOCALIZATION OF BRAIN TUMORS AND OTHER INTRACRANIAL LESIONS WITH RADIOACTIVE IODINATED HUMAN SERUM ALBUMIN

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LOCALIZATION of intracranial neoplasms with I^{131} as di-iodofluorescein or radioactive iodinated human serum albumin has been reported from 75 per cent to 95 per cent accurate. Davis, Martin, Ashkenazy, LeRoy, and Fields state that while the isotope study was over 90 per cent accurate, intracranial pneumography was only 63 per cent focally accurate and electroencephalography only 45 per cent focally accurate in their series. We have been unable to match this record of accuracy, but our study has shown the isotope method to be a useful adjunct to the diagnosis of some intracranial lesions. The results are very similar to those reported by Peyton, Moore, French, and Chou. The accuracy rate of each is about 75 per cent.

This investigation was carried out on 100 patients suspected of harboring intracranial neoplasms. Radioactive iodinated human serum albumin (RIHSA) was employed. The isotope in this form was chosen because it remains in the blood stream longer, permitting counts of the head from 10 to 24 hours after administration of the isotope and repetition of the counts several times if necessary. The patients for this study were taken from the neurologic and neurosurgical services of the New York Hospital. The isotope study was performed before any other diagnostic procedure such as intracranial pneumography or angiography, and interpretation was made without the clinical record.

METHOD

Five microcuries of RIHSA per kilogram of body weight were given intravenously. Lugol's solution was usually administered for several days to minimize the uptake of the radioactive iodine by the thyroid gland. The head was surveyed at 36 designated points 10 to 24 hours after the injection of the isotope. An elastic cap was used to mark out these points on the head. Some such device is essential for accurate results for it is often necessary to count several times over suspicious areas to be certain of the accuracy of the counting rate.

A shielded scintillation counter, a scaler, and recorder made up the instruments for measuring the concentration of the isotope.

The diagnostic work-up of these patients proceeded as indicated regardless of the outcome of the isotope study. With few exceptions, pneumoencephalography or pneumoventriculography and cerebral angiography were performed.

RESULTS

The correct prediction of the presence or absence of a neoplasm or other focal lesion was made in 76 out of the 100 cases (76 per cent). In order more fully to understand the limitations and advantages of the isotope method, the results will be presented under the following five headings: (1) normal or negative, (2) neoplasms of the cerebral hemispheres, (3) neoplasms in the posterior fossa, (4) vascular lesions of the cerebral hemispheres, and (5) miscellaneous. The results in the entire series are summarized in Table I.

Normal or negative (47 cases). The correct diagnosis of the absence of tumor or other focal lesion was made in 45 of these 47 cases, an accuracy rate of 95 per cent. The first of the incorrectly diagnosed cases was a young man with frontal headache and loss of visual acuity with general constriction of the visual fields. The counts in this man were high over the right frontal lobe and an erroneous diag-

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TABLE I.—RESULTS OF ISOTOPE LOCALIZATION IN 100 CASES

	No.	Per cent
Brain tumors, 41		
Correctly localized	25	61
Incorrectly diagnosed	16	39
Nontumors, 59		
Correctly diagnosed	51	86
Incorrectly diagnosed	8	14

nosis of a neoplasm was made. Subsequent pneumoventriculograms and bilateral carotid arteriograms were entirely normal. An exploration of the chiasmal region revealed arachnoiditis.

The second error in this group was a patient with psychomotor seizures. The counts in this man were quite high over the left temporal lobe, in which region a neoplasm was diagnosed. Subsequent pneumoencephalograms and carotid angiograms were entirely normal.

There appears to be no valid explanation for these two false-positive readings. However, the accuracy of the method is extremely high in excluding brain tumors as compared to the accuracy in the other groups of cases.

With electroencephalography there were 3 errors (false-positive) with 44 correct diagnoses, an accuracy rate of 93.7 per cent which is about the accuracy achieved by the isotope method.

Pneumoencephalograms and pneumoventriculograms were 100 per cent accurate. All of the cases are being followed, and there has been no change in the original figures thus far.

Neoplasms of the cerebral hemispheres (30 cases). Correct localization was made in 23 (76 per cent) of this group (Table II). As might be expected, the larger, more vascular lesions near the surface were best suited to detection by this method. Thus out of a combined total of 17 glioblastomas and meningiomas only 2 were missed. The first of these was a small glioblastoma deep in the frontal lobe. At operation a frontal lobectomy was performed before the lesion was identified. Pneumoventriculograms had clearly demonstrated the presence and position of the lesion.

TABLE II.—30 NEOPLASMS OF THE CEREBRAL HEMISPHERES

	No. of cases	Correctly localized	Missed
Glioblastoma multiforme	10	9	1
Astrocytoma	5	3	2
Meningioma	7	6	1
Metastatic	8	5	3
Total	30	23	7

The meningioma which escaped detection was a small tumor along the middle portion of the sphenoid ridge. Its presence and position were demonstrated by pneumoventriculography. The electroencephalogram correctly localized the glioblastoma multiforme but missed the meningioma.

In 1 case in this group the isotope study alone showed the presence of a parasagittal neoplasm. This patient was a 42 year old female who entered the hospital because of generalized convulsive seizures and headaches for 1 year. The electroencephalogram and pneumoencephalogram were negative. The isotope showed a distinct focus of increased uptake in the left parietal parasagittal region. Because of this finding a pneumoventriculogram was done which confirmed the presence of the parasagittal lesion. At subsequent craniotomy a 40 gram meningioma was removed.

The increase in counting rates over tumors ranged from 15 to 38 per cent. Table III shows the typical counting pattern over a large and vascular glioblastoma. The less vascular astrocytomas were not so well localized by this method. Also the smaller lesions of metastatic deposits were frequently missed. One of the metastatic tumors is of special interest. The patient was a 45 year old male who had a melanocarcinoma of the chest excised 4 years prior to his admission. He developed convulsions and weakness of the left arm and face over a 6 weeks' period. The isotope survey, pneumoventriculogram, carotid angiograms, and the electroencephalogram all were negative. On his seventh hospital day he suddenly lapsed into coma. An emergency craniotomy revealed a tiny deposit of melanocarcinoma in the motor area with a massive hemorrhage into the surrounding brain.

The limitations of isotope localization of cerebral neoplasms appear to be governed by avascularity and by the size and position of the tumor. An avascular tumor, regardless of

size and position, will not take up sufficient isotope for detection, while small tumors, regardless of vascularity or position, may defy detection.

The electroencephalogram was 50 per cent accurate and the pneumoventriculogram was 96 per cent accurate in this group.

Posterior fossa neoplasms (5 cases). There were 2 medulloblastomas, 2 acoustic neurinomas, and 1 cerebellar hemangioblastoma in this group. In only 1, a medulloblastoma, could correct localization be made and even in this case the increase in counting rate was borderline. Both acoustic neurinomas were subjected to repeated counts after access to the clinical data made the diagnosis almost certain. In spite of this a focus of increased counts over the neoplasm could not be found. The hemangioblastoma was a small tumor nodule in the wall of a large cyst. The isotope study showed a questionable focus in the right cerebellar hemisphere; the tumor, at craniotomy, was found in the left cerebellar hemisphere.

These findings would indicate that the isotope method is of limited value in posterior fossa lesions and further experience has confirmed this opinion. The reasons appear to be: (1) the relatively small size of the average neoplasm in the posterior fossa, (2) the heavy mass of overlying muscle, and (3) technical difficulties in positioning the counting tube.

Vascular lesions of the cerebral hemispheres (10 cases). Subdural hematoma (4 cases).— In all 4 cases the bulk of the hematoma was unilateral and it was possible to predict correctly the side and extent of the lesion in every case (100 per cent). The increase in counting rates was striking (20 to 30 per cent), and furthermore the area of increase was extensive, involving almost the entire half of the head (Table IV). No other lesion has produced this effect, and in later cases a specific diagnosis of subdural hematoma was made on the basis of the isotope survey. Exactly why there should be increased counting rates over a subdural hematoma is not clear. It is not due to an increased uptake by the hematoma itself, for the fluid actually contains far less of the isotope than venous blood. Perhaps a reasonable explanation would be that changes in the vascular bed of the brain occur secondary to the hematoma and permit "leakage" of the isotope into the substance of the entire hemisphere. At any rate, it appears from this small series that subdural hematomas can be localized by the isotope method.

TABLE III.—COUNTING PATTERN OVER GLIOBLASTOMA (CORRECTED COUNTS PER MINUTE)

	Left		Right		
	B	A	Midline	A	B
Prefrontal	4137	4249	4574	4274	4162
Frontal	4061	4189	4838	4699	4083
Central	4172	5154	5434	4451	3989
Post. temp.	6429	5908	5787	4478	4261
Parietal	5377	6198	5556	4759	4159
Occipital	6381	6331	5381	5259	4681

A & B represent anteroposterior lines along which counts are made, A being nearer the midline of the skull.

A large glioblastoma multiforme of the left posterior temporal, parietal, and occipital lobes. Note the great increase in counts in these areas.

Arteriovenous malformation (2 cases).— One of the lesions was correctly localized and another was missed. In both cases the patient was admitted to the hospital because of episodes of subarachnoid hemorrhage. The lesion which was missed was fairly small and close to the midline in the occipital pole. The correctly localized lesion involved the middle cerebral artery and was fairly extensive. Because of the abnormal and increased vascular bed of these malformations the isotope should be found here in higher concentration and permit localization.

TABLE IV.—COUNTING RATES OVER HEMATOMA (CORRECTED COUNTS PER MINUTE)

	Left		Right		
	B	A	Midline	A	B
Prefrontal	3681	3825	4500	4929	4897
Frontal	3521	3645	4681	5230	4673
Central	3501	3912	4767	5275	4705
Parietal	3406	4082	4771	5295	4850
P. Pariet.	3553	3901	4767	5057	4718
Occipital	3542	3694	4341	5143	4734

A & B represent anteroposterior lines along which counts are made, A being nearer the midline of the skull.

A large right subdural hematoma. Note increase in counts over the entire right hemisphere.

Thrombosis of major cerebral arteries (3 cases).—All of the cases were diagnosed by clinical signs and angiography. There were 2 cases of thrombosed internal carotid arteries; in one there was a questionable decrease in the number of counts over the ipsilateral anterior half of the head; in the other no change in the counting rate occurred. In both cases stellate ganglionectomy was performed and repeated isotope tests showed no change from the preoperative records.

In 1 case of thrombosed anterior cerebral artery there was no difference in the counts over the two sides of the head.

Thus, the isotope method would appear to be of little value in the study of cerebrovascular lesions. However, the collected experience is relatively small and final evaluation awaits a more extensive series.

Aneurysm of the anterior communicating artery (1 case).—The counting rate in this patient was normal.

Miscellaneous (5 cases). Pituitary tumors (3 cases).—Three chromophobe adenomas of the pituitary were all incorrectly diagnosed as normal. Repeated counts were made in 2 cases, but still a focus could not be found. The great distance from the counter, the small size of the tumors, and the mass of overlying cerebral tissue all contribute to the difficulty of localization.

Tuberculoma (1 case).—This was an occipital lobe lesion which was correctly localized and subsequently excised. The increase in the number of counts was similar to that found over neoplasms.

Chordoma (1 case).—This was a large lesion of the basisphenoid. It was impossible to detect any increase in activity attributable to the presence of the tumor.

CONCLUSION

Localization of brain tumors and other intracranial lesions with RIHSA is not only simple and easy to perform but is safe and relatively comfortable for the patient. It is somewhat time-consuming, requiring about 1 hour for each survey. The need for prestudy administration of iodine results in some delay before the isotope can be given, but in some instances when it has been necessary to save time iodine was not given. If the patient is in a reasonably good nutritional state there appears to be no serious risk.

The method is most valuable and accurate in neoplasms of the cerebral hemispheres. For neoplasms of the posterior fossa, pituitary tumors, and other small lesions about the base and in the midline, the method is of questionable value in its present stage.

Subdural hematomas can be consistently localized. The usefulness of the method in cerebrovascular lesions is yet undetermined.

The over-all accuracy of the method is better than electroencephalography, but not as good as pneumoventriculography. The results of this study show enough promise to justify continued investigation.

Improvement in the accuracy of this type of study would appear to depend on the development of another isotope more selectively concentrated in tumor tissue, plus a more sensitive and stable instrument for measuring radioactivity.

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A TEN YEAR ANALYSIS OF THROMBOEMBOLISM AND DICUMAROL PROPHYLAXIS

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POSTOPERATIVE venous thrombosis has been generally estimated as occurring in about 1 per cent of surgical patients and fatal pulmonary embolism in approximately 0.2 per cent. Various prophylactic measures have only sporadically and partially diminished the incidence of thrombotic and embolic episodes. Actually, Ochsner (11) has reported a progressive increase in the incidence of thromboembolism during the interval 1938 to 1949, together with an increase in the number of fatal pulmonary emboli. Indeed, fatal pulmonary emboli occur sufficiently often without previous warning (in at least 50 per cent of cases) to warrant the use of a simple, practical, preventive procedure. For obvious reasons, it is impossible to treat every postoperative patient with therapeutic amounts of anticoagulants. Spurred by 4 deaths from pulmonary embolism in this hospital between October 1942 and January 10, 1943 the coauthor decided to try the new drug dicumarol as a prophylactic measure against thromboembolism. The experiment was planned along conservative lines with the purpose of avoiding complications from the drug and the large amount of laboratory control which would otherwise be needed.

The prophylactic administration of dicumarol to women undergoing major abdominal, pelvic, and vaginal plastic surgery was initiated in this clinic on January 31, 1943. This report is an analysis of all cases of thrombophlebitis, phlebothrombosis, and nonfatal and fatal pulmonary emboli occurring during the 10 year interval ending January 31, 1953. Two previous reports have outlined the data through 1947 (17) and 1949 (16). Comparisons between dicumarol treated and similar untreated groups in the latter study gave some evidence that the drug had reduced thromboembolic complications during the period of its action.

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METHOD

The method of administration of dicumarol has varied according to the indications of clinical experience. For the first few months patients were given 200, 300, or 400 milligrams (depending on weight) the night before surgery. Thrombotic complications were more frequent. Therefore, between May 1943 and February 1947 most patients received the drug 1 to 3 days postoperatively and again 5 days later. To those still in bed a third dose was given on the eleventh or twelfth day. Those weighing over 60 kilograms received 200 milligrams and those weighing less, 100 milligrams. The third dose was 100 milligrams. One embolic death occurred before dicumarol was given. Therefore, from January 1947 on, the first dose, 100 or 200 milligrams, was given the night before operation and the second dose, 100 or 200 milligrams, 4 days later. Because of 2 deaths from embolism occurring 18 and 22 days, respectively, after the second dose, the decision was made in June 1949 to administer 100 milligrams every 4 days after the second dose to those patients still in the hospital. Not one of 2,850 women so treated from July 1, 1949 through January, 1953 has had pulmonary embolism. (Moreover, from January to October 1953, when this paper was submitted for publication, not one of 500 more patients so treated has had pulmonary embolism.)

During the early months of the study frequent determinations of prothrombin time were performed. In most women the amount of dicumarol administered caused an appreciable prolongation of the prothrombin time lasting 2 to 5 days. After 1944 the test was done once on each patient, usually on the

TABLE I.—TYPES OF OPERATIVE PROCEDURES (1947 TO 1952, INCL.) TOTAL 16,560

	Ward No. cases	Private No. cases	Total No. cases	
Hysterectomy	1529	1933	3462	25%
Radical hysterectomy	50	28	78	
Vaginal hysterectomy	450	356	806	
Suspensions	227	757	984	
Myomectomy	43	208	251	
Vulvovaginal*	2751	2309	5060	
Presacral neurectomy	80	368	468	
Herniorrhaphy	157	167	324	
Cholecystectomy	143	186	329	
Intestinal	168	116	284	
Urologic	84	73	157	
Pelvic evisceration	7	1	8	
Abdominoperineal	10	7	17	
Mastectomy	175	174	349	

*Includes anterior and posterior colporrhaphies done either alone or in association with abdominal or vaginal hysterectomy.

fourth or fifth postoperative day, to look for sensitivity or lack of effect. During the last 4 years no routine prothrombin determinations have been performed.

Patients having a past history of thromboembolic disease or severe varicosities have routinely had both legs snugly wrapped in ace bandages from ankle to midthigh as a preoperative measure. Elastic stockings have not been utilized. Most patients have been ambulated on the second to fourth postoperative day and have walked daily thereafter. In the early part of the study, however, they were not out of bed until the seventh or eighth day. Preoperative vein ligation has not been performed except in unusual circumstances.

MATERIAL

The cases for this study were those of ward and private patients who, for the most part, were undergoing major abdominal, pelvic, or vaginal plastic surgery. Almost 10 per cent of the operations were nongynecologic. A sample of the various operative procedures and the percentage incidence of hysterectomy are given in Table I. The treated series comprised ward patients and the private patients of the coauthor. The control series was made up of all private patients except those of the coauthor and 851 patients on the ward service in whom the drug was omitted for various reasons, e.g., request of operator, contraindication, and, most often, because they were under 40 years of age and apparently free of factors which predispose to thrombosis. All but 2 of the latter were in period I (Table III). During period II (Table III) the drug was not withheld from anyone because she was under 40 years of age. In both treated and control groups the preoperative and postoperative care was the same in all fundamental details; the anesthetists and anesthesias were the same and the surgery was performed in the same operating rooms. About 60 per cent of the surgery on ward patients was done by the resident staff.

Only cases of thromboembolism following surgery have been considered, and when this occurred over 30 days postoperatively the case was not included. There were no cases of pulmonary embolism after 30 days and only a few cases of phlebitis. Superficial phlebitis secondary to arm and leg venipunctures have similarly been excluded from the study.

THE ANALYSES

Yearly incidence of thromboembolic disease. Figure 1 outlines the yearly incidence of all thromboembolic cases, the 10 year total being 122. During this time there were 25,557 major and minor operations performed in the Free and Parkway Hospitals. The Parkway Hospital is the wing of the Free Hospital for Women for private patients. Excluding the ward patients in 1943, a rate of less than 1 per cent was maintained on both services. There were 6.0 thromboembolic complications per 1,000 operations in the Free Hospital (77 cases in 12,834 operations) and 3.5 per 1,000 in the private division (45 cases in 12,723 operations), the overall incidence being 0.48 per cent, which is low compared with other published figures.

Thrombophlebitis and phlebothrombosis. There were 63 cases diagnosed as either thrombophlebitis or phlebothrombosis in the Free Hospital (4.9 per 1,000) and 31 cases so diagnosed in the Parkway Hospital (2.4 per 1,000). Excluding cases of pulmonary embolism, the overall incidence in the entire series was 0.36 per cent. Fifty-seven of the ward and 11 of the private patients had received dicumarol prophylactically. The youngest patient was 32 years old, the oldest 71. Fifty-two of the cases followed complete hysterectomy with or without removal of adnexae. Twelve cases occurred after vaginal hysterectomy, 10 after vaginal plastics, 10 after gastrointestinal operations (excluding appen-

dectomies), and the remaining 10 after herniorrhaphies, radical hysterectomies, abdominal cervicectomies, and operations on the urinary system. Approximately three-quarters of the cases were classified as "deep" and the large majority occurred on the left side. Predisposing factors, noted in a high percentage of the cases, included varicosities of the saphenous system, history of previous phlebitis, obesity, anemia, pelvic hematomas, and cardiovascular disease.

Forty-four of the patients were treated with anticoagulants, 21 receiving heparin and dicumarol, 20 dicumarol alone, and 3 heparin alone. Twenty patients were treated surgically, 8 by interruption of the common femoral veins, 10 by division of the superficial femoral veins, and 2 by vena caval ligation. Nine patients were treated by elevation of the leg and application of heat. Five received only antibiotics and the remaining 16 had no specific treatment.

Nonfatal pulmonary embolism. There were 20 cases of nonfatal embolism during the 10 year period, 12 in the Parkway Hospital (0.9 per 1,000) and 8 in the Free Hospital (0.6 per 1,000). The overall incidence in the entire series was 0.078 per cent. The oldest patient was 69 and the youngest 37. Pulmonary emboli followed abdominal hysterectomy in 7 cases and vaginal hysterectomy in 4. Three occurred after vaginal plastics, 2 after cholecystectomies, and 2 after abdominoperineal resections. In 1 instance embolization followed a nephrectomy and in another occurred subsequent to a posterior colpotomy and drainage of multiple abdominal abscesses due to advanced rectal cancer. In 17 of the cases the initial symptom was chest pain, whereas 2 patients complained first of leg pain, and in 1 patient shock and cyanosis were noted without premonitory symptoms.

Of the 8 cases occurring in the Free Hospital, 6 had received prophylactic dicumarol (all before July 1949). The 2 omissions were at the request of the operator and through an oversight by the resident. Of the 12 cases in the Parkway Hospital, 2 had had the drug (before July 1949). Anticoagulant therapy was utilized as the primary therapeutic agent in 10 cases, whereas 8 patients were treated surgically—5 by superficial femoral vein interruption and 3 by caval ligation. Two patients received only penicillin.

Fatal pulmonary embolism. There were 8 deaths from pulmonary embolism among the 25,557 patients operated upon during the period of this report, an incidence of 1 in 3,194 cases, or 0.031 per cent. Six of the deaths were on the ward service, 0.046 per cent, and 2 on the private, 0.015 per cent. In 3 of the 8 cases an autopsy was not permitted, but the clinical picture was in each instance pathognomonic. On the basis of the total of 122 cases of thromboembolism, the mortality rate in this complication is 6.5 per cent. In 5 of the cases death occurred within a matter of minutes after the first warning, allowing no chance for treatment. In the other 3 there was an opportunity for treatment. These make the mortality rate, despite the chance for definitive therapy, 2.5 per cent.

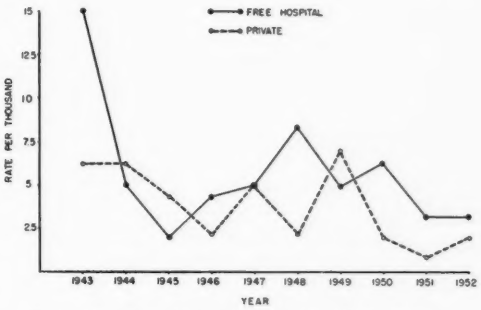

Fig. 1. Yearly incidence of thromboembolic disease.

The 8 deaths are outlined briefly:

CASE 1. 1944, Free Hospital, Mrs. W.S. (Unit No. 21,677). A 66 year old white female had a Manchester procedure because of cystocele, rectocele, and procidentia. No dicumarol was being given preoperatively at that time. Because of rather profuse bleeding during the operation, postoperative prophylactic dicumarol was omitted at the operator's request. She was allowed up on the ninth day, convalescence being entirely uncomplicated. On the tenth day she was found dead in bed. An autopsy revealed a massive embolus in the right pulmonary artery.

CASE 2. 1944, Free Hospital, Mrs. M.G. (Unit No. 24,065). A 39 year old white female had a resection of the sigmoid colon for adenocarcinoma together with a left salpingo-oophorectomy and cecostomy. The tumor was adherent to the left tube and ovary and the left common iliac vessels. On the first postoperative day she appeared in good condition but died suddenly without apparent cause. No dicumarol had been administered, since in 1944 the drug was not being given until the night of the first postoperative day or the morning of the second day. Autopsy was not permitted.

CASE 3. 1945, Free Hospital, Mrs. M.J. (Unit No. 25,962). A 57 year old white female had a complete hysterectomy and bilateral salpingo-oophorectomy and appendectomy for postmenopausal endometrial hyperplasia. Convalescence was uneventful. She was allowed out of bed on the seventh day. Shortly thereafter she complained of substernal pain. She became cyanotic and dyspneic and died 20 minutes later. Fifty milligrams of dicumarol had been given on the first and sixth postoperative days. An autopsy was not permitted. The reduction in dicumarol dosage had just been initiated because of a disturbing series of hemorrhages caused by or contributed to by the drug as indicated by excessively prolonged prothrombin times. Because of this death

TABLE II.—FREE HOSPITAL, BEFORE AND DURING DICUMAROL STUDY

	No. of thromboses	Incidence		No. of nonfatal emboli	Incidence		No. of fatal emboli	Incidence	
		Ratio	Per cent		Ratio	Per cent		Ratio	Per cent
1935 to Jan. 30, 1943 12,466 ward patients: before dicumarol study	138*	1:90	1.1	28	1:445	0.22	19	1:656	0.14
Feb. 1, 1943 to Jan. 31, 1953 12,834 ward patients: during dicumarol era	77*	1:166	0.60	8	1:1604	0.06	6	1:2139	0.05

*The number of thromboses includes those of embolism, both nonfatal and fatal.

the 100 and 200 milligram doses were at once resumed.

CASE 4. 1947, Parkway Hospital, Mrs. N.W. (Unit No. 35,731). A 73 year old white female had an exploratory laparotomy and biopsy of ovarian carcinomatosis. On the fifth postoperative day, following ambulation, she experienced a sudden attack of dyspnea and mild precordial pain. She was rapidly digitalized but anticoagulants were not given. Death occurred suddenly the next day. Autopsy revealed multiple pulmonary infarcts.

CASE 5. 1948, Free Hospital, Mrs. M.H. (Unit No. 39,139). A 48 year old white female had a radical hysterectomy and bilateral pelvic lymphadenectomy with partial resection of the rectosigmoid for squamous cell carcinoma of the uterine cervix. Her postoperative course was uneventful until the thirteenth day, when a pelvic cellulitis was discovered. She was allowed out of bed on the twenty-third day and shortly thereafter became cyanotic and dyspneic and went into shock. Fifteen minutes later she expired. Autopsy revealed emboli in the main pulmonary artery with acute cor pulmonale and thrombophlebitis of the right common and internal iliac veins. She had received dicumarol (100 milligrams) both the night before surgery and on the fifth postoperative day, but this was not continued despite delayed ambulation because of the possibility of hemorrhage in the large operative area. The drug has since not been withheld for this reason.

CASE 6. 1949, Free Hospital, Mrs. M.W. (Unit No. 39,835). A 57 year old white female entered the hospital complaining of postmenopausal bleeding and pelvic pain. She had a resection of the rectosigmoid, sigmoid colostomy, total hysterectomy, and bilateral salpingo-oophorectomy for what appeared to be obvious cancer involving these organs. The pathologic diagnosis was chronic granuloma, etiology unknown. Two hundred milligrams of dicumarol had been given preoperatively and 100 milligrams were given on the fourth day. Treatment was not maintained because the patient was being adequately ambulated. Wound dehiscence occurred on the eighth day through broken wire sutures. Secondary closure was performed immediately. On the twenty-second day, because of a deep phlebitis of the left leg, a bilateral common femoral vein ligation was done. The left superficial femoral vein was found to be completely occluded. Dicumarol was given (200 milligrams) on the day of ligation and again (100 milligrams) 2 days later, with the prothrombin activity reaching 30 per cent of normal. Death occurred 4 days following the vein ligation and 26 days after the primary surgery. Autopsy revealed a chronic pelvic peritonitis, phlebothrombosis of the left internal iliac vein with projection of the clot into the left common iliac vein. Emboli were found in branches of both right and left pulmonary arteries.

CASE 7. 1951, Free Hospital, Mrs. E.B. (Unit No. 27,040). A 72 year old white female had a loop colostomy for intestinal obstruction 4 years following a complete hysterectomy and bilateral salpingo-oophorectomy and x-ray therapy for carcinoma of the right tube. A ligation of the right saphenous vein had been done following this operation because of superficial thrombophlebitis. She did not receive preoperative dicumarol because of vomiting and the emergency nature of the operation. Prophylactic dicumarol was not given postoperatively but she was ambulated on the second day. On the seventeenth day she noted pain in the left thigh but was not treated. Later that day she became dyspneic and cyanotic and died shortly thereafter. Autopsy revealed a massive pulmonary embolus with thrombophlebitis of the left posterior tibial and popliteal veins together with primary adenocarcinoma of the rectosigmoid colon with obstruction. This was the senior resident's case. The coauthor has not made prophylactic dicumarol obligatory.

CASE 8. 1951, Parkway Hospital, Mrs. E.L. (Unit No. 48,817). A 55 year old white female had a colostomy and resection of the descending colon for advanced adenocarcinoma. Intestinal obstruction developed on the sixth day and routine measures with intubation were carried out. She was ambulated on the ninth day. On the twelfth day wound dehiscence occurred. On the nineteenth day she noted substernal pain, dyspnea, and orthopnea. Shock developed rapidly; papaverine and atropine were administered. Fifty milligrams of heparin were given subcutaneously and this was repeated every 3 hours. This dose was later increased to 75 milligrams when the clotting time did not exceed 6 minutes. On the twentieth day she had a recurrence of substernal pain and died 5 minutes later. Autopsy was not permitted. According to present opinion, the treatment with heparin was inadequate. Larger and intravenous dosage would seem to have been preferable and, if that failed to influence the clotting time, caval ligation might have been performed.

TABLE III.—SURGICAL PATIENTS, WARD AND PRIVATE, DURING DICUMAROL STUDY, COMPARISON OF PERIOD I AND PERIOD II

	No. of thromboses	Incidence		No. of nonfatal emboli	Incidence		No. of fatal emboli	Incidence	
		Ratio	Per cent		Ratio	Per cent		Ratio	Per cent
Period I Jan. 31, 1943 to June 30, 1949	86*	1:185	0.54	18	1:885	0.11	6	1:2657	0.04
15,943 patients	(58)‡			(8)			(3)		
Period II July 1, 1949 to Jan. 31, 1953	36*	1:267	0.37	2	1:4807	0.021	2	1:4807	0.021
9,614 patients	(21)‡			(0)			(0)		
Totals 25,557 patients	122*	1:209	0.48	20	1:1277	0.078	8	1:3194	0.031

*The number of thromboses includes those of embolism, both nonfatal and fatal.
‡The numbers in parentheses represent those of the group who had received dicumarol prophylactically.

The association of pulmonary embolism with carcinoma and its treatment is borne out in this study, 5 patients having had this disease in the sigmoid, ovary, cervix, rectosigmoid, and descending colon, respectively. The other 3 women were operated upon for procidentia, postmenopausal bleeding, and a pelvic mass (granuloma). The operative procedure in 5 instances involved resection of bowel and in 1 a colostomy. The other 3 patients had a Manchester operation, a simple total hysterectomy, and an exploratory laparotomy. In 3 cases the first symptom noted by the patient was chest pain; each had dyspnea. Two patients complained of leg pain and later developed chest pain and dyspnea. Two patients complained of leg pain and later developed chest pain and collapse. Two patients had no complaints, dying suddenly. One patient's sole difficulty was dyspnea prior to collapse.

Three of the 6 patients on the ward service who died of pulmonary embolism had not received dicumarol. In 1 case (Case 1) it was omitted because of excessive hemorrhage during surgery. The second case (Case 2) died on the first postoperative day, presumably of a pulmonary embolus, and since it was being administered in the evening of the first postoperative day at this stage of the study, she had not received any. The third case (Case 7) did not get it before operation because of intestinal obstruction. It was omitted during the postoperative period at the discretion of the resident surgeon. This is the patient who complained of thigh pain during the morning of the day she died but was not treated. Of the 3 patients who did get dicumarol 1 had only 50 milligram doses (Case 3). The other 2 (Cases 5 and 6) sustained their emboli on the twenty-second and twenty-sixth postoperative days, but it had not been administered after the fourth day in 1 case and after the fifth day in the other. One may only speculate as to whether 100 milligrams every fourth day might have prevented these fatalities.

Definitive treatment was given to only 1 of the 8 patients who died of pulmonary embolism. Three died within a matter of minutes after the onset of signs and symptoms and 2 died without premonitory evidence. One patient's (Case 4) precordial pain and dyspnea were misinterpreted as being of cardiac origin and digitalis was given. One woman (Case 7) complained of pain in the thigh on the morning of the seventeenth day, but this symptom was ignored. Intravenous heparin in large doses given immediately might have prevented this fatality. The only one (Case 8) who was treated received an inadequate amount of heparin.

Comparison of dicumarol treated and nontreated cases. In Table II the incidence of thromboses and embolism in the Free Hospital during the 8 year period immediately preceding the prophylactic use of dicumarol is compared with that during the 10 years of its use. Approximately 12,000 operations, major and minor, were done during each period. Thromboses were reduced by one-half, nonfatal emboli by over two-thirds, and fatal emboli by two-thirds during the dicumarol period.

TABLE IV.—INCIDENCE OF EMBOLISM IN MAJOR SURGICAL CASES 1943 TO 1953

	Nonfatal embolism	Fatal embolism
Control series No dicumarol		
Ward, 851 patients	2	3
Private, 5,035 patients	10	2
Total: 5,886 patients	12 (1:490) (0.20%)	5 (1:1177) (0.085%)
Treated series Received dicumarol		
Ward, 5,813 patients	6	3
Private, 892 patients*	2	0
Total: 6,705 patients	8 (1:838) (0.12%)	3 (1:2235) (0.045%)

*Patients of coauthor.

In Table III thrombotic complications during the interval February 1943 through June 1949, period I, are compared with those from July 1949 through January 1953, period II, when dicumarol was administered every 4 days for as long as patients were in the hospital and not withheld from those under 40 years of age. The figures for period II show considerable improvement, that for nonfatal embolism being statistically significant. During the 3 years and 7 months of period II pulmonary embolism did not occur in anyone prophylactically treated.[1]

In Table IV are compared 2 simultaneous series, each of approximately 6,000 patients, who underwent major surgical procedures. The treated group includes 5,813 ward cases and 892 private cases of the coauthor. The control series consists of 851 ward patients and 5,035 private patients. There was a diminution of nonfatal emboli from 1:490 in the control series to 1:838 in the treated series and of fatal emboli from 1:1177 to 1:2235. The better figures in the treated group are not statistically significant, but it should be recalled that the 3 deaths occurred in women who had not had either adequate or sustained dicumarol prophylaxis for the reasons stated in the case summaries (Cases 3, 5, and 6). The comparisons given in this section are in accord with the reports of Wise and associates, Allen and co-workers (2), and McCann, all of whom showed a reduction of thromboses and fatal embolism in prophylactically treated groups.

[1]No further embolism as of January 31, 1954 (4 years and 7 months).

DISCUSSION

Before 1943 the private patients of this hospital fared very little better than ward patients as regards thromboembolic complications. As controls in the present study, however, and contrary to expectation, they have not only shared with ward patients the overall decrease in these complications but have even fared better except for nonfatal embolism. The figures given in the early part of this paper, therefore, fail to show that dicumarol in addition to the usual prophylactic measures was of any especial value.

In comparing period I with period II (Table III), however, one cannot fail to be impressed by the better figures in the latter. During period II the drug was administered every 4 days for as long as patients were in the hospital, starting the night before operation. None of the 2,850 women so treated during this time or of the 500 so treated during the 8 months (to October 1953) since this period ended has had pulmonary embolism. Moreover, direct comparison of treated with untreated cases (Table IV) indicates that dicumarol was effective. The reduction in fatal embolism shown in this table would be very significant if the 3 cases of inadequate and unsustained treatment were listed as untreated, as we now consider them. But it was the experience with these very cases which brought about the changes in the method of administration and presumably the better results in period II and thereafter. Furthermore, examination of Table I reveals that a larger volume of more serious major surgery with its greater risk of thrombosis was performed upon ward patients and that, according to the larger numbers of uterine suspensions, myomectomies, and presacral neurectomies, considerably more of the private patients were younger and thus less prone to thrombosis. Although not unequivocal, the evidence strongly indicates that the prophylactic use of dicumarol in conservative dosage has been worth while.

The conservative dosage employed in this study and the lack of correlative prothrombin determinations are open to criticism. This is understandable, especially in view of the find-

ings of Lillie and associates, who noted that in only 10 per cent of their patients with normal pretreatment prothrombin levels was the prothrombin concentration reduced to 30 per cent of normal by a single 300 milligram dose. Conversely, in about the same percentage, 1,000 to 1,800 milligrams of the drug were necessary to secure an effective prothrombin range. We have suspected, however, that dicumarol may have effects on coagulation not measured solely by prothrombin determination. Pharmacologic investigations to date suggest that the anticoagulant effect of the drug is due chiefly to its suppression of prothrombin formation in the liver. This is probably not a simple competitive inhibition of vitamin K in prothrombin synthesis, although Wooley has suggested this as a possible mechanism because of the resemblance of the structural formula of vitamin K to that of dicumarol. Sandrock and Mahoney reported data concerning plasma prothrombin activity before and during surgery and for 6 days thereafter. They observed an increase in activity preceding the occurrence of clinical thrombosis, although at the time when thrombosis took place the prothrombin activity was usually normal or subnormal. Prophylactic dicumarol in low dosage may aid in the early depression of such increases in prothrombin activity. Experiments in man suggest that it also decreases an accessory clotting factor, possibly one of the plasma proteins which accelerate the conversion of prothrombin to thrombin. Ochsner and associates (12) have suggested that blood hypercoagulability is associated with a relative disproportion between the prothrombin and antithrombin levels. Low antithrombin concentrations, it is believed, predispose to intravascular clotting. Dicumarol perhaps directly enhances antithrombin activity. An increase in the number and then destruction of platelets following surgical procedures have been demonstrated. Dicumarol does not, so far as is known, diminish the platelet count, but a significant decrease in platelet adhesiveness has been observed in blood removed from rabbits and humans made hypoprothrombinemic with it. Although speculative, it may, even in low dosage, have this effect on in vivo clotting.

TABLE V.—MORTALITY FOLLOWING THERAPEUTIC MEASURES IN THROMBOEMBOLIC DISEASE

	Author	Year	No. of cases	Embolic deaths	Mortality percentage
Anticoagulants	Murray*	1947	520	0	0.00
	Bauer*	1950	351	3	0.85
	Jorpes*	1950	445	7	1.50
	E. V. Allen*	1950	681	1	0.15
	Evans‡	1952	1716	8	0.46
	König	1951	76	2	2.6
Totals			3789	21	0.55
Femoral vein interruption	A. W. Allen*	1952	1937	10	0.52
Anticoagulants and surgery	Free Hospital	1953	122	3	2.5

*Cited by Allen (1).
‡Personal communication (4).

Complications must be anticipated when dicumarol is used, especially when over 6,000 patients have received it. Allen (1) described 2 deaths directly due to hemorrhage from it. So far as can be determined, specific sensitivity with marked prolongation of the prothrombin time and bleeding therefrom have occurred in only 8 women. One of these patients had rheumatic heart disease with moderate decompensation and in 2 others excretion was possibly delayed because of diminished renal function. There were no deaths attributable to the drug. It has been used in patients with all degrees of cardiovascular disease without complications. (The cases found to be hypersensitive were satisfactorily treated with vitamin K_1 oxide and fresh blood. The injection of potent vitamin K_1 compounds in patients with thromboembolic disease is not without some hazard and may predispose to sudden fatal embolism. It may be wiser here to give transfusions of fresh blood to control bleeding while maintaining a relatively low prothrombin level.) Thus our failure to have routine determinations of prothrombin time performed has not resulted in serious or frequent hemorrhagic complications. On the other hand, it undoubtedly resulted in not finding those who required larger doses and hence developed possibly preventable thromboses.

The 0.031 per cent incidence of fatal embolism in the present series (ward and private) is low compared with previous experience in

this hospital, a sample of which is shown in Table II. The figure is lower than any of those cited by Gage in his "survey of reported incidence of pulmonary embolism and thrombosis, 1889 to 1951." Pratt and associates reported 23 cases of fatal pulmonary embolism occurring in 17,742 gynecologic operations from 1926 through 1950, an incidence of 0.12 per cent, which is about the same as the incidence in this hospital prior to the clinical experiment with dicumarol. On the other hand, Phaneuf cited only 1 fatal embolus in 6,530 gynecologic procedures at the Carney Hospital in Boston from 1941 through 1951, an incidence of only 0.01 per cent. And Bauer had an incidence of only 0.013 per cent in a series in which heparin had been used prophylactically.

Our mortality rate in cases of thromboembolism in which there was an opportunity for treatment leaves something to be desired, since there were 3 deaths in 122 cases, 2.5 per cent. As shown in Table V, this is considerably higher than the rates reported from general surgical services, although it is the same as that recently reported by König from a gynecologic service.

It is interesting that dicumarol has replaced prophylactic superficial femoral vein ligation at the Massachusetts General Hospital in those prone to develop thromboembolism. Thromboses in such a series were reduced to 20 per cent of those in a control series. As regards prophylactic surgery, the coauthor has on occasion in recent years included bilateral ligation of the internal iliac vessels during pelvic operations in women suspected of being predisposed to thrombosis. The postoperative courses were normal. In 2 of our 8 cases of fatal embolism the clot was demonstrated to have come from the internal iliac veins.

The treatment of patients with thrombosis is now being carried out in this clinic with intravenous, intermittent, large doses of heparin, as advocated by Jorpes, until the prothrombin time can be reduced to 30 per cent of normal by dicumarol. In the presence of nonfatal pulmonary embolism, the authors had come to believe that ligation of the vena cava was the only sure therapy. Gage has recently stated unequivocally that the vena cava should be ligated in all cases with nonfatal pulmonary embolism. Yet Murray reported a series of 149 such patients among a total of 520 (Table V) treated with anticoagulants alone without a fatality. As shown in Table V, his results were exceptional, there being a considerable mortality in the other reported series despite the employment of anticoagulants therapeutically. The decision between caval ligation and anticoagulants in nonfatal pulmonary embolism remains difficult.

SUMMARY

1. Dicumarol, in conservative doses with some and then no laboratory control, has been given prophylactically to 6,705 of 25,557 women undergoing surgery from February 1943 to January 1953, inclusive. Hemorrhagic complications were infrequent and without mortality.

2. During this 10 year clinical trial there were 8 deaths from pulmonary embolism, 0.031 per cent, and 20 cases of nonfatal pulmonary embolism, 0.078 per cent. These and 94 instances of thrombosis without embolism make a total of 122 cases of thromboembolism, 0.48 per cent. These figures reflect a marked improvement over previous experience in this hospital and are low compared with most of the figures surveyed in the literature.

3. Although the use of dicumarol could not be demonstrated conclusively to have been of value, the various comparisons and considerations presented strongly indicate that it was a factor in achieving the improved figures.

4. Since July 1949, dicumarol has been given every 4 days starting the evening before operation for as long as patients remained in the hospital. None of 3,350 women so treated to October 1953 has had pulmonary embolism.[1]

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[1]From July 1, 1949 to January 31, 1954, 4,044 patients have received dicumarol prophylactically. No emboli have occurred in this group. During the same period 1 fatal and 8 nonfatal emboli have occurred in an equal number of untreated cases.

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A MODIFICATION OF THE GALLI MAININI PREGNANCY TEST USING SERUM AND THE DIFFUSION ENZYME HYALURONIDASE

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THE Galli Mainini pregnancy test has been used in the pregnancy diagnostic unit in the Huddersfield Royal Infirmary for 2½ years. This test consists in the injection of either the concentrate of 50 cubic centimeters of urine (concentration by Scott's method) or the injection of 2 to 3 cubic centimeters of untreated morning urine into the dorsal lymph sac of the male toad. The toad is then catheterized 1 to 3½ hours later and its urine examined for the presence of spermatozoa, the presence of which is indicative of chorionic gonadotrophins in the patient's urine.

This test, using the English male toad, Bufo bufo, and the Asian toad, Bufo viridis, as the test animal, gave an accuracy of 99.1 per cent in the first year and 99.9 per cent subsequently, the total number of tests to date being nearly 4,000.

Quantitative tests are performed by extracting a series of different volumes of urine, by measuring the time taken for the animal to respond to the injection, and by sperm counts. It is thought that although a combination of these methods gives an accurate quantitative result for a given specimen of urine, it is probable that this is an inaccurate reflection of the amount of hormone in the blood, since the volume of morning urine is dependent upon such variable factors as fluid intake, habit, and renal function. It seemed reasonable, therefore, that the use of sera or plasma would not only eliminate these factors but would also avoid the time-consuming procedure of detoxification of grossly contaminated specimens as well as give further positive advantages to be discussed later. These fluids were tried, therefore, a number of times, but the results were usually extremely poor, and the effects upon the toads often devastating. For example, negative tests were obtained in the sera of patients known to be pregnant and with positive urine tests; and the toads became limp, anuric, and often died before the completion of the test. These results correspond with those of R. W. Marsters and his associates who found that many test animals (Rana pipiens) died, and all became depressed when injected with human sera.

This article is a preliminary report on how this problem can be solved by the addition of the diffusion enzyme hyaluronidase to either serum or plasma. Preliminary tests using hyaluridase only failed to cause a spermatokinetic response. Further, hyaluronidase, when added to urine or urine concentrates, was found not to influence either the test time or the test result. Tests were then carried out with hyaluronidase and serum, firstly to find the volume of serum or plasma which would give a positive test in the shortest possible time, the amount of enzyme remaining constant, secondly to find the amount of hyaluronidase which would cause quick diffusion, thirdly to find the volume of water to add to the hyaluronidase, and finally to ascertain the most suitable injection volume of the sera-hyaluronidase preparation which would give the best result with the least trauma to the toads. It was found that a 2:1 ratio was suitable, i.e., 1 cubic centimeter of serum or plasma to 0.5 cubic centimeter of hyaluronidase prepared by adding 1 cubic centimeter of distilled water to a 3 milligram ampule of this substance.

The ideal injection volume appeared to be 0.25 cubic centimeter of the sera-hyaluronidase mixture, as 0.5 cubic centimeter did not give better results, indeed burdened the animals with more protein, and 0.1 cubic centimeter often increased the test time considerably.

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A series comparing the respective merits of serum and plasma, using the same blood specimen, gave conflicting results, but on the whole the results using sera were more uniform and also had the advantage that no special tubes were needed for the collection of the specimens.

METHOD

Three to 5 cubic centimeters of blood are required to give an adequate volume of serum or plasma for full quantitative estimations to be made. To 1 cubic centimeter of serum is added 0.5 cubic centimeter of hyaluronidase (prepared as already indicated). A Mantoux syringe is loaded with 0.5 cubic centimeter of this mixture and 0.25 cubic centimeter is injected slowly into the dorsal lymph sac of each of 2 animals, the remaining fluid being injected in amounts of 0.1 and 0.05 cubic centimeter into further animals should quantitative tests be required. If it is necessary to obtain the results at once, the animals are then catheterized every 5 minutes and the urine examined for sperm, but routine tests can be read at half-hourly intervals or once at the end of 2½ hours according to the convenience of the worker.

Fifty-two patients clinically pregnant and with positive urine tests were investigated by this method, the duration of pregnancy ranging from 4 to 36 weeks. Of the 52 patients, 39 (75 per cent) gave positive serum tests in from 10 to 30 minutes, and 13 (25 per cent) took longer. Six of these last were positive within 1 hour, 6 within 2 hours, and 1 patient who was aborted within the next 2 weeks and who had a low titer of hormone in the urine, 2 hours and 20 minutes (Fig. 1).

Further, it was found that in early pregnancy (3 to 4 weeks) the test time in 2 patients was less than 1 hour, in pregnancies of 6 to 16 weeks ½ hour or less (10 minutes in 1 patient), the average being 15 minutes, and in 4 patients investigated after 23 weeks less than half an hour (average 20 minutes). These test times are thus in inverse proportion to the titer of chorionic gonadotrophins known to be present in pregnancies of this duration. It is of interest that the patient with a positive serum test in 10 minutes had a twin pregnancy and that a positive test was obtained with as little as 0.001 cubic centimeter of serum.

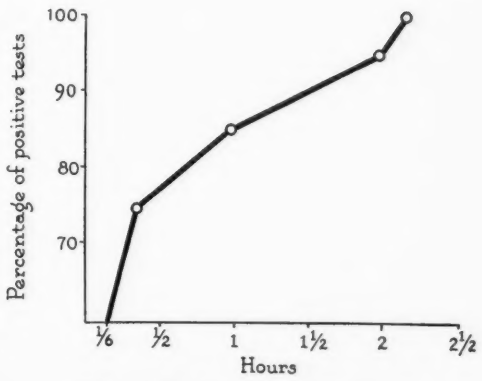

Fig. 1. Graph showing test time response.

DISCUSSION

It has long been felt that urine, as the test fluid for pregnancy, has many disadvantages. Untreated urine may be either so toxic to the toads as to reduce their sensitivity for further frequent quantitative tests, or, it may kill them outright, thus necessitating the repetition of the test and the purchase of new animals. A further and a more serious disadvantage in using untreated urine is that the titer of the hormone in the urine may be so low that false negative results are obtained as, for example, in low titer chorionepithelioma. Although Scott's method of detoxification and concentration excludes such errors, especially in animals of high sensitivity, it has the disadvantage that it is time-consuming, which may be serious when large numbers of tests need to be done at one time.

Plasma or serum seem to present no such disadvantages and are certainly not toxic when used as already indicated (0.25 c.c. for routine tests and less for quantitative tests). The animals, providing they are well to start with, suffer no ill-effects from these tests, will be found able to self-feed the day after injection, and are quite ready for further injections after a week's rest.

Further, quantitative tests are easy, and low titer specimens are not missed since the

titer in the serum is vastly higher than in the urine. From the patient's point of view, the rapidity of the tests is an advantage, and the possibility of having a pregnancy test done as quickly as a blood count is now a reality in 75 per cent of cases. The disadvantages of venipuncture or a finger prick would seem to be small compared with the advantage, both to the patient and the doctor, in having the results of tests available the same morning as the patient attends the outpatient department.

From the laboratory point of view, the ease and rapidity of the test are excellent, and the time which is spent in detoxifying urines and in looking after sick animals as well is very materially reduced.

SUMMARY

A modification of the Galli Mainini test for pregnancy is described using serum or plasma as the test fluid and hyaluronidase to decrease the test-time and to minimize the toxic effects upon the animals.

Fifty-two patients clinically pregnant and with positive urine tests for chorionic gonadotrophins were investigated. Of these, 39 patients had positive serum tests in from 10 to 30 minutes, 6 within 1 hour, 6 within 2 hours, and 1, who had a very low titer both in the urine and in the serum and who was to abort 2 weeks later, had a positive test in 2 hours and 20 minutes.

It is suggested that the ease, accuracy, and rapidity of the test, and the lack of toxic effects upon the animals commend it for general use.

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EXPERIMENTAL ESOPHAGOGASTRECTOMY: RELATION OF TYPE OF RESECTION TO DEVELOPMENT OF ESOPHAGITIS

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EXTENSIVE resections for lesions of the cardia and esophagus are now not only technically feasible but can be carried out with a reasonably low mortality rate. As a result, the surgeon's attention is being directed more and more to the secondary effects of such operations. If radical surgical procedures are to be advised for carcinoma of the cardia and esophagus in the hope of cure, the high morbidity rate that accompanies such procedures must be reduced.

One of the common complications of esophagogastrectomy as now performed is esophagitis. This complication is probably due to regurgitation of acid gastric juice into the esophagus. The extreme sensitivity of the esophageal mucosa to the effects of acid gastric contents has been demonstrated experimentally. Several factors favor regurgitation following esophagogastrectomy. These include the elimination of the esophagogastric junction and the diaphragmatic pinchcock mechanism and the formation of a new esophagogastric junction within the thorax. In addition, vagotomy leads to pylorospasm, gastric atony, and gastric retention. Which of these factors plays the major role in regurgitation cannot be stated at present. There is, however, ample experimental evidence to show that surgical procedures which destroy or by-pass the cardiac mechanism lead to regurgitation of acid gastric contents and to subsequent development of esophagitis.

Medical measures to combat this complication are of limited clinical value. Any operation which might eliminate this complication or reduce its incidence would be of considerable value. Because of the lack of an operative method for adequately restoring the cardiac mechanism, an operation which reduces the amount of acid gastric contents which could regurgitate into the esophagus seems logical. With this end in view, Wangensteen (7) and Womack and associates (10) advocated resection of all the acid-secreting portion of the stomach and an esophagoantral anastomosis in cases of cardiospasm. Wangensteen added pyloromyotomy to this procedure to offset undesirable effects of vagotomy. Their results have been reported as satisfactory.

Our studies were carried out to determine the relative incidence of esophagitis after different types of esophagogastrectomy.

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METHODS

Adult mongrel dogs varying in weight from 6.5 to 18 kilograms were used. Esophagogastrectomy was carried out under intravenous pentobarbital sodium anesthesia in amounts of 25 milligrams per kilogram of body weight. The lungs were aerated by intermittent positive pressure delivered through an intracheal tube. The left side of the chest was opened through the ninth intercostal space. The caudal portion of the esophagus was mobilized and both vagi were ligated and divided. Mobilization of the stomach was carried out through an opening in the diaphragm which extended from the esophageal hiatus to a point 2 to 3 centimeters from the lateral diaphragmatic attachment to the chest wall. The left gastric artery was ligated and divided, and the stomach was devascularized down to the point chosen for resection. Approximately 1 to 2 centimeters of the distal portion of the esophagus was resected in all cases.

The amount of stomach resected in the different groups is shown diagrammatically in Figure 1. In groups 1, 3, and 4, a small amount of the acid-secreting portion of the

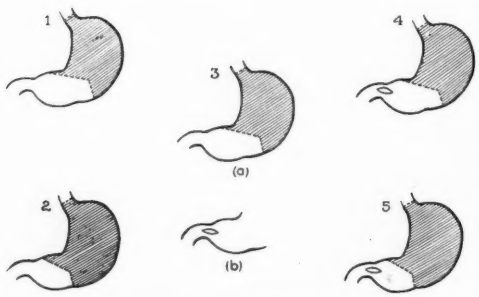

Fig. 1. The operative procedures and amount of stomach resected are represented diagrammatically in this illustration. Shaded areas indicate the amount of stomach resected.

stomach was left intact. The method of esophagogastrectomy described by Kirklin and Clagett was employed. A clamp was placed across the stomach at right angles to the greater curvature at a point 2 to 3 centimeters proximal to the antrum. The amount of stomach included in this clamp was designed to equal the circumference of the esophagus. After partial division of the stomach above this clamp, another clamp was placed at an angle downward from the end of the first clamp to a point on the lesser curvature proximal to the pylorus so that a large portion of the lesser curvature of the stomach was included in the specimen removed. The lesser curvature side of the stomach included in the second clamp was closed with two rows of continuous catgut sutures and an outer row of interrupted silk sutures. A tube of remaining stomach was then available for anastomosis to the esophagus. It was estimated that not more than 80 per cent and not less than 70 per cent of the acid-secreting portion of the stomach was resected by this technique.

In groups 2 and 5, the stomach was transected at the proximal level of the antrum in order to remove the entire acid-secreting portion of the stomach. A small segment of the lesser curvature portion of the antrum was removed also in these two groups in the process of forming a tube of antrum for anastomosis to the esophagus.

A two layer anastomosis was made between the esophagus and stomach. The outer layer was closed with interrupted silk sutures, and the inner layer in some animals was closed with a continuous catgut suture and in others with interrupted silk sutures.

An extramucosal type of pyloromyotomy was performed in groups 3, 4, and 5. A long incision was made over the antrum, pylorus, and duodenum and all the structures superficial to the mucosa were carefully incised so that the pyloric sphincter was effectively divided and the mucosa pouted out through the incision.

The diaphragm was closed and the new esophagogastric junction was placed well within the thorax by attaching the stomach to the diaphragm with a few interrupted silk sutures.

TABLE I. — ESOPHAGOGASTRECTOMY AND ESOPHAGITIS IN DOGS

Group	Operation			Results at necropsy			Duration of survival, days*
	Per cent of acid-secreting stomach removed	Pyloromyotomy	No. of dogs	Esophageal ulcer	Esophagitis	No esophagitis	
1	70–80	0	8	5	3	0	8 died 19–115 d. (av. 59.5)
2	100	0	6	0	1	5	5 died 28–94 d. (av. 50.8) 1 killed 288 d.
3	70–80	+ delayed	4	2	1	1†	4 died 50–99 d. (av. 66.5)
4	70–80	+	6	3	3	0	4 died 56–147 d. (av. 89.5) 2 killed 122 and 127 d.
5	100	+	8	0	2	6	2 died 23 and 25 d., 6 killed 95–137 d. (av. 110.1)

*Duration of survival after esophagogastrectomy.
†This animal had esophagitis earlier.

Postoperatively, the dogs received nothing but water by mouth for 2 to 3 days. They were then given 1 feeding a day of standard kennel ration. No attempt was made to encourage the dogs to eat by offering them frequent meals of specially prepared and appetizing food.

RESULTS

A total of 32 dogs was used. Five different groups were studied and the results are tabulated in summary form in Table I.

Group 1. Eight dogs underwent esophagogastrectomy with removal of approximately 70 to 80 per cent of the acid-secreting portion of the stomach. Pyloromyotomy was not performed in this group. Vomiting was a constant postoperative feature in these animals and they all lost weight and eventually died of inanition and malnutrition. Death occurred from 19 to 115 days after operation, the average length of postoperative survival being 59.5 days. All dogs showed evidence of acid peptic erosion of the esophagus at postmortem examination. Linear esophagitis was present in 3 of the 8 dogs. Definite esophageal ulcers were present in the 5 remaining dogs. In 1 animal the ulcer had perforated into the mediastinum. The ulcers occurred regularly on the right lateral wall of the esophagus just at the suture line. The appearance of 1 of these ulcers which is typical for all is shown in Figure 2. Of the 6 animals surviving longer than 1 month, all but 1 had esophageal ulcers.

Group 2. In 6 dogs the entire acid-secreting portion of the stomach was removed and the esophagus was anastomosed to the antrum. Pyloromyotomy was not performed in this group. With 1 exception these dogs all vomited postoperatively, lost weight, and eventually died from inanition and malnutrition from 28 to 94 days after operation. One animal maintained its weight and nutrition and was killed by an overdose of pentobarbital sodium 288 days after operation. No esophageal ulcers developed in this group of dogs. One animal which died 61 days after operation had mild esophagitis. The postmortem appearance of the esophagus in 1 of the 5 dogs that showed no esophageal changes is illustrated in Figure 3.

Fig. 2. Esophageal ulcer present at postmortem examination 56 days after esophagogastrectomy with removal of 70 to 80 per cent of the acid-secreting portion of the stomach.

Group 3. Esophagogastrectomy with removal of 70 to 80 per cent of the acid-secreting portion of the stomach was carried out on 4 dogs as in group 1. Approximately 4 to 6 weeks later the development of esophagitis or esophageal ulcer was demonstrated in all 4 dogs by esophagoscopic examination. Pyloromyotomy was performed on all of these dogs. Its purpose was to ascertain whether addition of a procedure to facilitate gastric emptying could reverse the esophageal changes that had already developed after esophagogastrectomy.

Vomiting and loss of weight followed esophagogastrectomy in this group as in groups 1 and 2 and continued unchanged after pyloromyotomy. The dogs died 50 to 99 days after esophagogastrectomy and 17 to 56 days after pyloromyotomy. The average length of survival was 66.5 days after esophagogastrectomy. The esophagus of only 1 dog was free of esophagitis at postmortem examination.

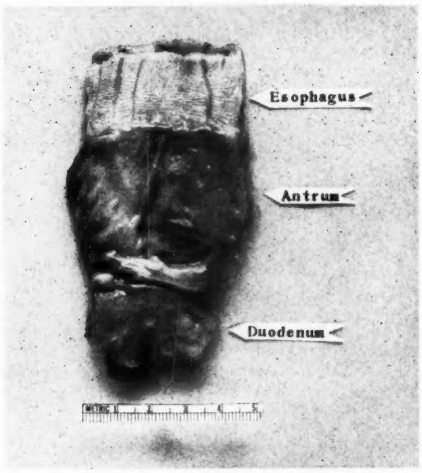

Fig. 3. Normal-appearing esophagus at postmortem examination 9 months after esophagogastrectomy with removal of the entire acid-secreting portion of the stomach and anastomosis of esophagus to antrum.

Esophagoscopy had shown a definite esophageal ulcer and esophagitis in this dog at an earlier date. Of the remaining 3 dogs, 2 had esophageal ulcers, and 1 dog had esophagitis with an area of superficial esophageal erosion.

Group 4. Concomitant esophagogastrectomy and pyloromyotomy was performed on 6 dogs. Seventy to 80 per cent of the acid-secreting portion of the stomach was resected as in groups 1 and 3. Vomiting occurred in some of these animals but was not as severe as it was in the preceding experiments. Four dogs eventually died of inanition but their survival time (average 89.5 days) averaged a month longer than that of the dogs in groups 1 and 2. Two animals maintained their nutrition well and were killed by an overdose of pentobarbital sodium 122 and 127 days after operation. All dogs showed evidence of esophageal erosion. One or more esophageal ulcers were found at postmortem examination in the distal part of the esophagus of 3 of these 6 dogs (Fig. 4). In 1 of these 3, the ulcer had perforated into the mediastinum. Esophagitis (Fig. 5) was present in the remaining 3 dogs. In 1 dog, the esophagitis was severe and had led to hemorrhage from which the animal apparently succumbed.

Group 5. Eight dogs underwent concomitant pyloromyotomy and esophagogastrectomy with removal of all the acid-secreting portion of the stomach. The esophagus was anastomosed to the antrum. Postoperative vomiting was not a major problem in this group of dogs. All the animals lost weight but not as markedly as those in groups 1 to 3. Two dogs died 23 and 25 days after operation. Postmortem examination failed to reveal esophagitis or the cause of death. The remaining 6 dogs were killed by an overdose of pentobarbital sodium from 95 to 137 days after operation, the average length of postoperative survival being 110.1 days. A mild, but not significant, degree of linear esophagitis was seen in the postmortem specimens of 2 dogs. Esophageal ulceration did not occur.

COMMENT

Before the results of a study such as this are analyzed, it must be emphasized that certain differences between man and the dog make it difficult to transfer findings for the dog directly to human beings. The usual position of a dog's esophagus and stomach is more horizontal than vertical and the gravitational factors which favor regurgitation of acid gastric contents into the esophagus are different from those in man. Dogs tend to bolt a large bolus of food. In the absence of a large pouch to receive the food the tendency to regurgitate is greater than in man who can be instructed to take small feedings at frequent intervals. No effort was made to feed our animals small amounts of specially prepared food, and the early death of many of the dogs was the result of vomiting followed in time by malnutrition and inanition. The fact that esophageal ulcers or esophagitis developed at some time after operation in all the dogs which retained acid-secreting stomach following esophagogastrectomy does not coincide with the incidence of this complication in human beings who have undergone similar operations. In spite of these differences, the results of these studies may have some clinical bearing.

The now well recognized sensitivity of esophageal mucosa to the damaging effects of acid gastric contents is again indicated by our results. Only when all of the acid-secret-

ing portion of the stomach was removed was significant esophagitis successfully prevented. Admittedly, gastric secretory studies were not carried out in these experiments. Conclusive evidence that acid stomach contents caused the observed esophageal changes will depend on such studies. Topete and co-workers stated that when the vagus nerves are divided in the dog at the time of esophagogastrectomy, esophagitis does not develop, whereas such changes are encountered only when the vagus nerves are left intact. In another study by Kiriluk and Merendino (3) of the effects of esophagogastrectomy on dogs, fewer esophageal changes were noted when the vagus nerves were left intact than when vagotomy was performed. In the studies reported herein, vagotomy was performed on all the dogs in association with esophagogastrectomy and severe esophagitis and esophageal ulcers developed in many of them.

The constant location of ulcers on the right lateral wall of the esophagus at the anastomotic line is worthy of special comment. No explanation is available for this finding but it suggests that the maximal concentration of acid gastric contents is directed toward the right lateral wall of the lower part of the esophagus during regurgitation and vomiting. However, in the absence of definite proof of acid peptic etiology of these ulcers, this should be considered no more than hypothesis. Esophageal ulcers have been described in the presence of achlorhydria and the possibility of trophic factors has been considered in the etiology according to Womack.

Pyloromyotomy or pyloroplasty is not generally performed on patients undergoing esophagogastrectomy. Pyloromyotomy, however, has been suggested when this operation is employed in the treatment of cardiospasm. Pyloroplasty has been advocated by Wangensteen (8) when segmental gastric resection is performed for duodenal ulcer with anastomosis of antrum to cardia. It is now generally agreed that a drainage procedure of some type should be carried out on the stomach when vagotomy is performed for duodenal ulcer because of the pylorospasm, gastric atony, and retention of secretions which follow vagotomy alone. It seems only logical to include such a procedure when esophagogastrectomy is performed, for the remaining portion of the stomach is effectively vagotomized after esophagogastrectomy and the capacity of the gastric remnant is necessarily small.

Fig. 4. Esophageal ulcer at postmortem examination 61 days after esophagogastrectomy with removal of 70 to 80 per cent of the acid-secreting portion of the stomach and a concomitant pyloromyotomy.

Kiriluk and Merendino (2) stated that neither pyloromyotomy nor pyloroplasty reduced the incidence of vomiting in dogs undergoing esophagogastrectomy with removal of 50 per cent of the acid-secreting portion of the stomach. Sauvage and his associates concluded from experiments in dogs in which the antrum was anastomosed to the cardia following formation of a fundic pouch that preservation of the diaphragmatic muscle fibers around the esophagus prevented vomiting to a great extent. They also stated that the addition of pyloromyotomy was of benefit in this regard.

Although vomiting did occur in some of our dogs that underwent pyloromyotomy in association with esophagogastrectomy, it was not as severe as it was in animals on which this procedure was not carried out. Furthermore, maintenance of weight and good nutri-

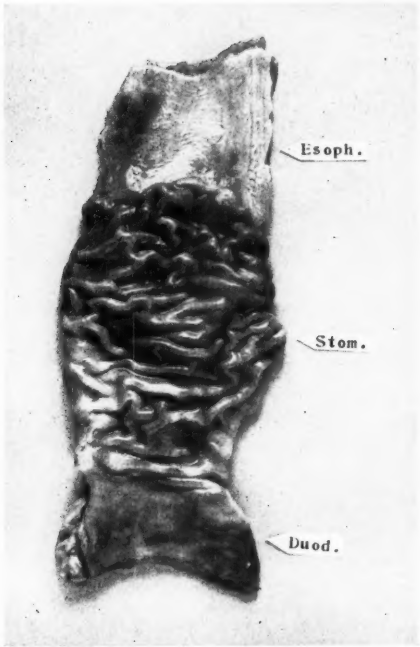

Fig. 5. Esophagitis at postmortem examination 4 months after esophagogastrectomy with removal of 70 to 80 per cent of the acid-secreting portion of the stomach and concomitant pyloromyotomy.

tion was better and survival was longer in those experiments which included pyloromyotomy. This procedure, however, did not prevent the development of esophagitis or esophageal ulcers when acid-secreting stomach remained, nor did it consistently reverse these changes once they had occurred after esophagogastrectomy. Kiriluk and Merendino (3) reported that gastrojejunostomy will not prevent the development of esophagitis following esophagogastrectomy when acid-secreting stomach remains. They achieved better results in avoiding peptic esophagitis after such procedures by the creation of a crude valvelike esophagogastrostomy. The best results in our animals were obtained when all of the acid-secreting portion of the stomach was removed and pyloromyotomy was performed concomitantly. Six of the 8 dogs undergoing this operation survived and were in a fair state of nutrition when they were killed. None of the 8 had esophagitis of significant degree. Furthermore, this procedure did not lead to severe esophagitis from the regurgitation of alkaline duodenal contents into the esophagus like that reported after esophagoduodenostomy by Cross and Wangensteen. Wangensteen (8) warned against performing a Heineke-Mikulicz type of pyloroplasty when the antrum is anastomosed to the esophagus for fear of the development of esophagitis following regurgitation of alkaline duodenal contents into the esophagus. This type of pyloroplasty was not performed on our animals.

We have already advised caution in applying the results of these experiments to the management of clinical cases. Nevertheless, it seems advisable whenever possible to remove all of the acid-bearing portion of the stomach and to perform pyloromyotomy or some type of a drainage procedure on the stomach when esophagogastrectomy is carried out. Pyloromyotomy was the only such procedure used in these experiments. It will be necessary to assess the value of other procedures aimed at facilitating gastric emptying. The operation, as outlined herein, would have limited clinical application and would have to be reserved for the management of lesions of the cardia and the lower end of the esophagus. Resection of lesions higher in the esophagus would not permit such an extensive resection of the stomach. However, the same conclusions regarding the desirability of carrying out concomitant pyloromyotomy should apply irrespective of the level of the lesion or the extent of the resection.

CONCLUSIONS

The development of esophagitis in dogs is directly related to the amount of acid-secreting stomach removed. By removal of all the acid-secreting portion of the stomach, the development of significant degrees of esophagitis is prevented.

The addition of an extramucosal pyloromyotomy does not protect against the development of esophagitis after esophagogastrectomy when acid-secreting stomach remains, nor will it consistently cause a reversal of this change once it has occurred.

Pyloromyotomy performed at the same time as esophagogastrectomy reduces the incidence and severity of postoperative vomiting, allows better nutrition, and permits longer survival of dogs after esophagogastrectomy.

Pyloromyotomy done in association with esophagogastrectomy and anastomosis of the esophagus to the antrum does not lead to significant degrees of esophagitis from the regurgitation of alkaline duodenal contents into the esophagus.

In these experiments the most satisfactory type of esophagogastrectomy consisted of resection of all the acid-secreting portion of the stomach together with concomitant extramucosal pyloromyotomy.

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OBSERVATIONS ON THE PATHOLOGY OF PRIMARY CARCINOMA OF THE VAGINA AND ITS RELATION TO THERAPY

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KNOWLEDGE of behavior of tumors is based largely on observation of large numbers of cases in various stages, and on pathologic studies of surgical specimens and autopsy material. It is only when this information is available that treatment can be applied intelligently and a prognosis given in realistic terms. Primary carcinoma of the vagina is an example of a neoplastic disease in which this knowledge is deficient. Possibly because of this, the response to treatment of various types has been almost uniformly poor and, what is also bad, in many instances unpredictable. This ignorance is due partly to the rarity of the condition and also to the scarcity of suitable pathologic material. Postmortem studies are of limited value, since the terminal stages of the disease reveal little concerning its earlier behavior and resistance to treatment. There have been no detailed reports of the surgical pathology of primary carcinoma of the vagina in its early phases.

The low incidence is such that it is often quoted in a ratio to the occurrence of carcinoma of the cervix, the usual figure being 1:35 or 1:45 of the latter tumor. A more realistic idea of how often the condition is encountered may be gained from the recent report of Messelt from the Norwegian Radium Hospital. Since virtually every carcinoma of the vagina discovered in Norway is referred to this institution for treatment, he was able to state that in any given year 1 carcinoma of the vagina would be found for every 160,000 females in the country over 25 years of age. If this ratio is applicable to the adult population of New York City, only about 35 new cases would be discovered in the city annually. In a discussion of the subject in 1948 Stanley Way commented that "a study of the literature reveals a state of almost universal despondency." He believed that the principal reason for lack of progress in the treatment of carcinoma of the vagina was "almost complete ignorance of the clinical behavior of this rare form of cancer." Perhaps in response to this statement, six studies have appeared subsequently, reporting in aggregate 506 cases in this country and abroad (Table I). For the most part these are tabulations of recorded data over a considerable period of time, and therefore represent clinical observations in an indirect form. These statistics show that carcinoma of the vagina occurs, in the average case, early in the sixth decade, and that there is no direct relation of the disease to race, economic status, or family history. There is no consistent relation to the presence of trauma or irritating conditions. No precancerous stage or definite predisposing factors have been found. The results reported in these papers differ little from those of earlier years, despite a variety of therapeutic methods. It is only fair to state, however, that the majority of these cases were seen before the advent of modern radiologic and surgical procedures.

As Table I shows, surgical treatment of the disease has been employed infrequently. The extensive dissection necessary and the excessive operative mortality discouraged this approach until recent years. In many of the recorded cases, operation consisted merely of local extirpation of the tumor followed by radiation treatment. Little attention has been devoted to study of these specimens. As a result we have only indirect information regarding the early stages of the disease; its mode, route, and rate of spread; and rela-

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tively little data on the topography and histologic appearance of the tumor.

During the period 1944 to 1952, 7 patients with proved primary carcinoma of the vagina were admitted to the Gynecological Service of Bellevue Hospital. During this period there were 17,259 admissions, including 471 instances of carcinoma of the cervix. The incidence of vaginal carcinoma was .04 per cent, and the ratio of vaginal to cervical carcinoma, 1:67. All cases of vaginal carcinoma were treated surgically, and the operations were individually planned as curative rather than palliative procedures. Together with a single case from the University Hospital, this material is the basis of the present study.[1]

Pelvic exenteration with vulvectomy was carried out in 1 case. Radical hysterectomy was performed 4 times, and vaginal hysterectomy once; in 2 other cases the uterus had been removed previously. In addition to the exenteration operation, removal of the bladder was done in 2 cases. The rectum was excised in 1 case for a recurrence following the primary operation. Total colpectomy was carried out 3 times, and partial colpectomy (with removal of most of the vagina) 5 times. In 1 of the latter cases further removal of vaginal tissue was necessary. Dissection of the parametrial, obturator, hypogastric, and external iliac nodes was done in 6 cases. Inguinal node dissection was attempted once, but abandoned because of the patient's precarious condition. In most cases, therefore, the operation was sufficiently radical to provide definite information regarding the pathology and spread of the disease.

In 5 cases the operative specimen was fixed before sectioning, and in 2 cases additional studies were made from fixed material which had been cut previously. Sections were made from the primary tumor to show its relationship to underlying and adjacent structures, particularly the rectovaginal septum, bladder, cervix, and neighboring vagina. Routine blocks were taken from the cervix, uterus, tubes, and ovaries. All lymph nodes were sectioned, and in 2 cases clearing the tissues in propylene glycol resulted in the discovery of additional lymphoid tissue for study.

[1]Case 8 is used through the courtesy of Dr. Gray H. Twombly.

TABLE I.—PRIMARY CARCINOMA OF THE VAGINA IN THE RECENT LITERATURE

Author	Period	Cases No.	Radiation No.	Surgery No.	Survival per cent
Way 1948	1930–1946	44	27	6	18.2
Livingstone 1950	1925–1946	110	93	14	10.5
Huber 1950	1922–1949	152	63	14	17.0
Singh 1951	1925–1949	21	16	3	0
Messelt 1952	1932–1945	78	78	0	22.7
Kaiser 1952	1927–1950	55	41	6	13.0
Bivens 1953	1931–1951	46	38	4	27.5
	Totals	506	356	47	

Survival—5 year absolute survival rate.
Surgical treatment in many instances consisted of local excision only.

CLINICAL DESCRIPTION

The pertinent clinical details of these cases are summarized in Table II and are similar to those reported in other studies. Case 5 seems worthy of discussion, however, since it represents an unusual instance of carcinoma of the vagina under observation from its early stages. This patient was seen by her local doctor for the complaint of "burning sensation" in the vagina. A suspicious area was noted in the posterior fornix near the cervix, which was not ulcerated or indurated. A biopsy of the cervix failed to reveal carcinoma. Six months later the patient was admitted to Bellevue with a complaint of vaginal bleeding for 4 months. At this time she had a tumor mass filling the upper half of the vagina, involving the posterior and both lateral walls. Removal of the tumor required an exenteration operation and vulvectomy.

GROSS TUMOR CHARACTERISTICS

The classification of these tumors has been made largely from clinical descriptions, with some implications as regards mode of spread and rapidity of growth, but with little correlation to prognosis. From the description of Healy, three forms are recognized: everting, or papillary carcinomas; infiltrating, or inverting carcinomas; and surface tumors. Instances of all three types were found in the present series (Table III).

Everting tumors. This appears to be the most common type, according to the literature, outnumbering other forms by 2 or 3 to 1.

TABLE II.—CLINICAL DATA

Case	Age, years	Parity	Symptoms	Findings	Treatment	Course
1 F.A. 1944	56	1	Bleeding 8 months, previous supracervical hysterectomy	1 by 1.5 cm. mass, posterior wall, lower ⅓	Vulvectomy; partial colpectomy	Recurred 6 months Abd.-perineal resection done Alive and well 8 years
2 C.S. 1948	70	?	Bleeding 3 weeks	4 cm. mobile mass, lateral wall, upper ⅓	(1) Local excision (2) Vaginal hysterectomy partial colpectomy (3) Inguinal node dissection	Alive and well 4 years
3 H.R. 1952	39	1	Postcoital bleeding, 2 years, staining, 3 months	3 cm. indurated area, posterior fornix	(1) Radical hysterectomy; pelvic node dissection; partial colpectomy (2) Excision of remaining vagina	Alive and well 1 year
4 M.M. 1952	56	8	Bleeding 2 months	Ulcerated lesion, upper ⅔ ant. wall; bladder wall involved	Radical hysterectomy; cystectomy; colpectomy; pelvic node dissection	Died 8th postoperative day; shock, pulmonary embolus
5 C.F. 1952	34	2	Discharge 6 months, bleeding 4 months	4 by 6 cm. mass upper ⅓ posterior and lateral walls	Pelvic exenteration; vulvectomy; colpectomy; ureterocutaneous transplantation	Alive 6 months, pyelonephritis
6 L.C. 1952	48	3	Dysuria, 6 months bleeding, 6 weeks	Ulcerated lesion upper ⅔ anterior wall; bladder wall involved	Radical hysterectomy; cystectomy; colpectomy; pelvic node dissection; ureterointestinal anastomosis	Alive and well, 3 months
7 P.S. 1952	70	2	Bleeding, 6 months, previous hysterectomy	3 by 4 cm. mass, posterior wall upper third	Partial colpectomy; pelvic node dissection	Alive and well, 2 months
8 Mu.M. 1952	47	0	Discharge, 3 months, bleeding 2 months	3 by 5 cm. mass, posterior wall upper ⅓	Radical hysterectomy pelvic node dissection; partial colpectomy	Bladder recurrence, radiation therapy, died 5 months

It is characterized by a papillary or polypoid outgrowth of tumor tissue from a broad or sessile base, with clearly demarcated edges. The tumor may reach large size, filling or even distending a portion of the vaginal canal while remaining mobile, so that clinically it may seem attached only to mucous membrane. In all but 1 case in the present series, ulceration with consequent infection and bleeding had occurred. Inflammatory reaction in underlying tissues may simulate tumor invasion on clinical examination. Five cases of this type were found, 4 arising in the posterior vaginal wall and 1 on the right lateral wall (Figs. 1 and 2).

TABLE III.—GROSS PATHOLOGIC FINDINGS IN RELATION TO BLEEDING

Case	Form	Location	Size, cm.	Duration of bleeding
1 F.A.	Everting	Posterior wall lower ⅓	1×1.5	8 months
2 C.S.	Everting	Lateral wall upper ⅓	4×4	3 weeks
3 H.R.	Surface tumor	Posterior wall upper ⅓	3×4	2 years (3 months)
4 M.M.	Infiltrating	Anterior wall upper ⅔	4×5	2 months
5 C.F.	Everting	Posterior and lateral walls upper ⅓	4×6	4 months
6 L.C.	Infiltrating	Anterior wall upper ⅔	5×7	6 weeks
7 P.S.	Everting	Posterior wall upper ⅓	4×4	6 months
8 Mu.M.	Everting	Posterior wall upper ⅓	3×5	2 months

There were no fistulas in this series.
In Cases 4 and 6, both infiltrating tumors of the anterior wall, the bladder wall was invaded.

Infiltrating tumors. The inverting or infiltrating form of vaginal carcinoma is usually regarded as carrying a much less favorable prognosis. Infiltration of submucosal tissues and attachment to neighboring structures occur much earlier, and due to lateral growth beneath the surface epithelium, ulceration seldom indicates the true extent of the lesion. Two carcinomas of this variety were found in this material. Both were extensive tumors of the anterior vaginal wall, infiltrating the wall of the bladder, but with little ulceration of the bladder mucosa. While the number of

cases included here is too small to be cited as evidence, the relation of tumor form to location may be valid in view of anatomic considerations to be discussed later. The principal characteristic of this tumor form is downgrowth with little or no projection of the tumor into the vaginal lumen (Figs. 3 and 4).

Surface tumors. Rare instances of carcinoma, which is virtually limited to the surface epithelium and rapidly encircles the vaginal canal, have been described. Similar cases have been reported in which the tumor arose from the cervix. This tumor form is referred to in the German literature as *zuckergusskrebs*, and has been successfully treated in some instances by the local application of radium alone, a procedure which may be compared with local excision. One tumor of this type was found, arising in the posterior fornix. Its full extent was not appreciated on clinical examination, and studies of the surgical specimen left doubt as to whether the tumor had been completely removed. While biopsies of the remaining vagina were negative, positive cell smears were obtained and further removal of vaginal wall was carried out, amounting to a total colpectomy. Neither ulceration nor induration is a prominent finding in this tumor form. The involved mucous membrane has a roughened, pebbled appearance with whitish areas suggesting hyperkeratosis. This is borne out microscopically (Fig. 5).

Table III shows the relation of tumor form and size to the duration of symptoms. Aside from rapid growth, which is well illustrated by the clinical observations in Case 5, it would appear that carcinoma of the vagina often reaches considerable size without ulceration and consequent bleeding. This is best illustrated by Case 2, in which a 4 centimeter everting tumor produced vaginal bleeding on only 1 occasion 3 weeks before admission for another complaint. In this respect carcinoma of the vagina is even more dangerous than carcinoma of the cervix, in which the lack of correlation between extent of disease and duration of symptoms is well known.

There were no fistulas in this series, although in both of the anterior wall carcinomas invasion of the bladder wall had occurred. This is in accord with the findings of Kaiser and Way that fistulas represent a late stage in the disease.

Fig. 1. Case 5. Pelvic exenteration. The top of the bladder and the posterior wall of the rectum have been cut away from the specimen. There is a large everting tumor of the posterior vaginal wall which distends the vagina but has not penetrated the muscularis to involve the rectum.

MICROSCOPIC CHARACTERISTICS

All of the tumors studied were of the squamous cell variety. The microscopic features are similar in many respects to those of squamous cell carcinoma in other locations, particularly of the cervix. Most of the attention devoted to this subject in the past has had to do with histologic grading of the tumors, using a system of the type described by Broders. As in the case of carcinoma of the cervix, this suffers from the difficulty of finding uniform and representative fields of tumor tissue, as well as the problem of correlating these findings with clinical outcome of treatment. The description which follows is di-

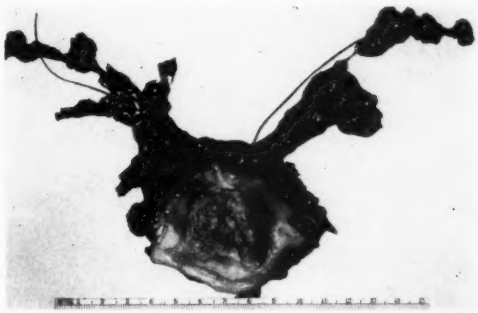

Fig. 2. Case 7. Colpectomy and pelvic node dissection. There is a discrete, everting tumor in the upper third of the posterior vaginal wall. The patient had had a total hysterectomy previously.

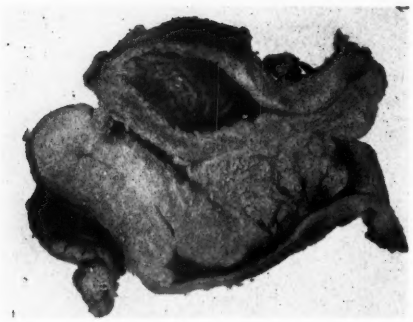

Fig. 3. Case 4. Radical hysterectomy, colpectomy, cystectomy, and pelvic node dissection. Infiltrating tumor of the anterior vaginal wall, involving the bladder.

rected mainly at the morphology of the tumor, with the aim of discovering what relation this may have to gross appearance and spread of the disease (Table IV).

Microscopic architecture. In 4 instances, all everting tumors of the posterior vaginal wall, the growth was *papillomatous* (Fig. 6). It was made up of greatly thickened folds and furrows of squamous epithelium, projecting upward from the surface with limited invasion at the base. Three tumors were *infiltrating* in type, and in 2 of these this was in accord with the gross tumor form. Here there was little upward growth, as a rule, but marked downgrowth and lateral spread beneath intact surface epithelium (Fig. 7). The single instance of surface carcinoma was flat and for the most part intraepithelial in extent. A few areas of beginning invasion were noted, but there was neither deep downward pegging nor papillomatous growth above the surface. The thickness of the tumor in its most extensive portion was about twice that of normal vaginal epithelium (Fig. 8).

Fig. 4. Case 6. Radical hysterectomy, colpectomy, cystectomy, and pelvic node dissection. Infiltrating tumor of the anterior vaginal wall with bladder involvement. Tumor extended far beyond the margins of vaginal ulceration.

Mode of invasion. Schiller has observed that carcinoma of the cervix seldom shows invasion of the underlying tissue by single cells or small groups of cells but rather by large strands of malignant tissue with well demarcated edges. In 2 of the papillomatous vaginal carcinomas invasion occurred by this cord-like downgrowth; these were 2 of the best differentiated tumors in the series (Fig. 9). In the remaining cases however, downgrowth by single cells and cells in small strands and clumps was noted in what might be described as diffuse invasion. This may be related to the consistency of the subepithelial tissues; the vaginal wall is far more elastic than the cervical stroma and is comparable to the wall of the stomach, where diffuse invasion commonly occurs (Fig. 10).

Lateral growth. This refers to lateral spread of the tumor either along the surface epithelium, or to subepithelial spread without consistent loss of the covering mucous membrane. The former condition in its most extensive form is illustrated by the single case of surface carcinoma. Sections show intraepithelial carcinoma extending far beyond the limits of the tumor on gross inspection. Marked lateral extension below the surface was noted in both of the infiltrating tumor types, and this was suspected in the gross specimen by the presence of induration considerably beyond the ulcerated tumor margins. Lateral surface growth was noted also for a short distance in 1 of the everting tumors.

Transition zones. The presence of a marginal "belag" of intraepithelial carcinoma between the invasive tumor and normal squamous epithelium was noted twice. In the remaining cases the transition was abrupt or was obscured by ulceration beyond the margin of the tumor.

Differentiation. The tumor was well differentiated in 3 cases, all everting, papillomatous tumor forms, with no fixation to underlying structures. Although the cells along the invading margin were of an undifferentiated

basal type, elsewhere there was extensive keratinization and occasional pearl formation. Stratification into layers, with a clearcut honeycomb layer containing numerous apparently normal cells, was observed overlying and contiguous with actively invasive carcinoma. Hyperkeratosis of the adjacent nonneoplastic epithelium was frequently noted, with some hyperplasia of the basal layers (Fig. 11). Two tumors showed slight or moderate degrees of differentiation, one of these being infiltrative in form and the other surface spreading. The remaining tumors were undifferentiated and in some cases markedly anaplastic with bizarre cell forms. Of the latter, 2 were everting carcinomas and 1 infiltrating.

Contact spread. In 2 specimens there were separate areas of carcinoma in tissues which were directly opposed to the primary lesion, and in contact with it. The intervening mucous membrane was normal in appearance. This phenomenon may be explained either as contact spread of the neoplasm, spread by mucosal lymphatics, or as multicentric origin. In view of the intimate situation of the lesions in both instances, contact spread appears to be the logical explanation.

Tissue reaction. Edema and infiltration of underlying tissues by leucocytes were absent or very slight in the case of surface carcinoma. Moderate or slight infiltration by lymphocytes and plasma cells in the tissues immediately adjacent to the advancing tumor edge was noted in 4 of the 5 everting tumors, all papillomatous. Marked reaction with large fields of polymorphonuclear leucocytes was noted in 2 cases, both rapidly growing infiltrating tumor forms which were poorly differentiated (Fig. 10).

Lymphatic involvement. Involvement of mucosal lymphatics and small lymphatics at the margin of the tumor was often seen (Fig. 12). However, it was noted that in no instance was tumor found in the deeper lymphatics, or in the smaller lymphoid collections or nodes in the areolar tissue adjacent to and peripheral to the vaginal muscularis. Moreover, no tumor was found in the parametrial or pelvic nodes in any of the 6 specimens in which these tissues were available for study. In 3 cases there was evidence of old or recent inflammation in the parametrial nodes.

Fig. 5. Case 3. Cervix and upper vagina showing a surface carcinoma. The black area of the anterior lip of the cervix is the result of injection of india ink, used in this case as an aid in the delineation of pelvic lymphoid tissue. The roughened, white area in the posterior fornix is surface carcinoma, and a separate area of contact spread is seen on the posterior lip at 6 o'clock.

Involvement of adjacent structures. Once the absence of remote spread was demonstrated, examination of the advancing edge of invasive tumor showed it to have a distinct margin, easily demonstrated under low power. In both of the infiltrating tumors of the anterior vaginal wall penetration had occurred with invasion of the bladder wall. In tumors situated on the posterior vaginal wall, however, displacement and distention of the vaginal muscularis by the tumor were present, and despite the considerable size of some tumors grossly, there was no instance of penetration of the

Fig. 6. Case 2. Everting tumor, papillomatous type. This is a well differentiated tumor with little invasion of the muscularis despite its size (4 cm. in diameter). Adjacent squamous epithelium shows basal cell hyperplasia and hyperkeratosis. ×5.3.

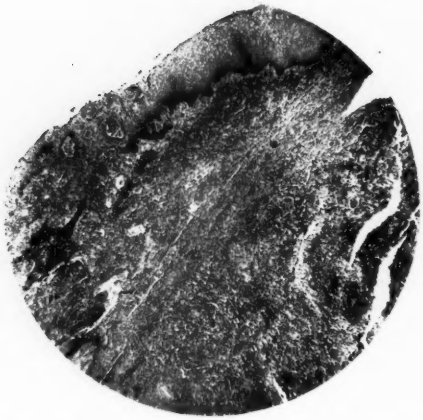

Fig. 7. Case 4. Infiltrating tumor of anterior vaginal wall. Diffuse invasion of muscularis with lateral spread beneath normal stratified squamous epithelium. ×18.7.

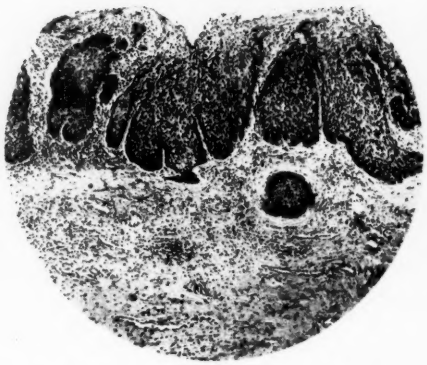

Fig. 8. Case 3. Surface tumor. Widespread involvement of vaginal mucous membrane with early invasion of underlying tissues. In most areas basal membrane is intact. ×37.5.

underlying fascia. Rectal involvement occurred in a single case near the anal orifice, as a recurrence following local excision, which obviously was inadequate.

ANATOMIC CONSIDERATIONS AND LYMPHATIC SPREAD

It is often stated that the abundant lymphatic and vascular supply to the vagina is a paramount factor in the rapid growth and spread of the disease. In most large series on record, it is stated that half or more of the patients exhibited clinical evidence of spread beyond the local lesion when first seen, the spread often occurring by way of lymphatic channels to regional nodes. This is thought to explain, in part, the poor results which have been obtained by various forms of treatment. These observations were based largely on clinical examination rather than biopsy evidence or examination of surgical specimens.

The lymphatic circulation of the vagina has been described by Rouviere. Small channels are found in the subepithelial tissues and muscular wall of the vagina, anastomosing to form collecting branches in the areolar tissues surrounding the vagina, which run upward along the lateral walls. In the upper half of the vagina these are said to drain to the same nodes which serve the uterus: the parametrial, obturator, hypogastric and iliac chains. In the lower half of the vagina anastomoses occur with the channels draining the vulva, to the inguinal and femoral nodes. The lymphatics

TABLE IV.—MICROSCOPIC PATHOLOGIC FINDINGS

Case	Gross form	Location	Microscopic architecture	Invasion	Lateral growth	Transition zone	Differentiation	Contact spread	Tissue reaction
1	Everting	Posterior wall	Papillomatous	Cords	0	Abrupt	Well	0	Moderate
2	Everting	Lateral wall	Papillomatous	Cords	0	Gradual	Well	0	Slight
3	Surface tumor	Posterior wall	Flat, surface spread	Slight	Marked	Gradual	Moderate	Yes	0
4	Infiltrating	Anterior wall	Infiltrating	Diffuse	Marked	Abrupt	Poor	0	Marked
5	Everting	Posterior wall	Infiltrating	Diffuse	0	Abrupt	Poor	0	Marked
6	Infiltrating	Anterior wall	Infiltrating	Diffuse	Moderate	Abrupt	Moderate	0	Moderate
7	Everting	Posterior wall	Papillomatous	Diffuse	0	Abrupt	Well	0	Moderate
8	Everting	Posterior wall	Papillomatous	Diffuse	Moderate	Abrupt	Poor	Yes	Moderate

Fig. 9. Case 1. Invasive carcinoma with downgrowth of large cords and masses of malignant cells. There is only mild reaction of the surrounding tissue. ×37.5.

Fig. 10. Case 4. Diffuse invasion. Carcinoma cells are seen singly and in small strands, and there is marked edema and inflammatory reaction in surrounding tissues. ×56.

of the upper vagina may also anastomose with those of lower canal, which is occasionally shown by inguinal nodes bearing metastases from cancer located in the vaginal fornices.

As previously stated, the parametrial and pelvic nodes were available in 6 of the 8 cases studied. In the remaining 2 cases, survival for 8 and 4 years respectively furnishes indirect evidence that these nodes were not involved at the time of operation. The failure to find regional node metastasis in any of these cases was a distinct surprise, for node involvement was suspected in several cases on clinical examination. Moreover, it was confidently expected in view of the concept of early lymphatic spread of the disease. The clinical findings in these suspicious cases must be explained by evidence of inflammation in the pelvic nodes, probably secondary to inflammatory changes in the vagina adjacent to the tumor.

This series is too small to permit a conclusive statement regarding the frequency of lymphatic spread to regional nodes, and the stage of the disease at which it occurs. However, it would appear to be less frequent, and a later manifestation, than is currently believed. The implication is clear that complete surgical removal of the tumor with a good chance of cure is often feasible, even when the primary lesion is large and involves neighboring structures.

Another gross and microscopic observation was of considerable interest. Even in the largest and most extensive tumors, downward invasion seemed to involve the interstices of the muscular wall of the vagina and to distend it for a considerable distance before penetration occurred. The well known elasticity of the vaginal wall, particularly of the posterior wall, appears to favor this course, so that thickening and induration of the vagina are by no means synonymous with penetration into neighboring structures. This is well illustrated by the specimens of Cases 5 and 8, tumors of the posterior fornix. These tumors, while virtually filling the upper vagina, had not penetrated the muscularis of the organ grossly or microscopically. In the latter case involvement of the rectal wall was suspected, but at operation it was evident that penetration had not occurred and the rectum was not removed. In both cases, despite the large size of the primary tumor, no involvement of the lymphatics or areolar tissues between rectum and vagina was found.

In the anterior wall the tendency of the tumor to confine itself temporarily to the muscular wall of the vagina is not so obvious, and in both cases in this series extension into the bladder was evident, probably due to the decreased mobility and elasticity of the vaginal tissues beneath bladder neck and urethra.

Fig. 11. Case 7. Everting papillomatous tumor of the posterior vaginal wall. The margin of the malignant process is discrete, and there is no penetration of the muscularis. ×6.5.

CLINICAL STAGING

In an effort to evaluate results of radiation therapy, a number of authors have adopted arbitrary clinical stages similar to those in use in carcinoma of the cervix. Like the League of Nations classification, this scheme suffers in practical use from the fact that spread beyond the primary site cannot be confirmed by biopsy in the majority of instances. For this reason, series of cases treated by radiation can never be classified as exactly as those subjected to surgery. In fact, as will be seen, the former group may be classified most erroneously.

For example, the clinical stages prescribed by Courtial are as follows: stage I—tumor limited to the vagina and involving not more than half of the wall from which it arises; stage II—tumor extending over more than half of the anterior or posterior vaginal wall, with paravaginal soft tissue infiltration, but without demonstrable involvement of bladder or rectal mucosa; stage III—tumor infiltrating the rectal, bladder, or urethral mucosa, extending to the vulva, or with fixation to pelvic bone. Courtial had 3 cases in stage I, 11 cases in stage II, and 8 cases in stage III. Employing a similar classification, Bivens recently reported 4 cases in stage I, 23 cases in stage II, and 13 cases in stage III.

If the cases in this series are ranked according to this classification, 2 would fall into stage I, 4 in stage II, and 2 in stage III. Following pathologic study, however, all of the stage II cases are relegated to stage I. The thickening and induration of the rectovaginal septum and parametrial tissues which would have placed half of this series in stage II was found to be inflammatory in nature.

While the need for some such system in the clinical evaluation of radiation therapy results is recognized, its faults should be understood and it should never be used as criteria for operability.

DISCUSSION

Three gross forms of vaginal carcinoma have been described which correspond to the clinical categories already in use, and which appear to have certain microscopic characteristics. The everting form is usually found on the posterior vaginal wall, seldom shows lateral growth, and may reach considerable size and distend the vaginal wall without deep invasion. Microscopically these are usually papillomatous growths which are well differentiated. The rate of growth and spread as judged by tissue reaction is probably slow as compared to other forms of vaginal carcinoma. The infiltrating form occurred only on the anterior vaginal wall in this series. It is an anaplastic, poorly differentiated tumor with considerable lateral spread, and little growth outward into the vaginal lumen. A third, and rare, form of tumor is described, the surface carcinoma. This tumor is largely confined to the mucous membrane, with marked lateral growth and little invasion. Its extent is difficult to judge on clinical examination.

When the gross pathologic findings and clinical description of these tumors are compared with the duration of symptoms, it is apparent that carcinoma of the vagina is a rapidly growing neoplasm which may reach large size without producing symptoms. In view of its rarity, it is unlikely that any sizable number of these cases will be found in the early stages; the only reliable means of early detection would be routine periodic examina-

tion at shorter intervals than now recommended in the postmenopausal age group.

Of great clinical interest is the finding that on microscopic examination the tumor extended beyond the described vaginal limits in 4 of the 8 cases, either by surface or subepithelial lateral spread. This necessitated further operation in 1 case. Similar experiences are reported by Kaiser (Cases 1 and 4).

The failure to find parametrial and pelvic lymph node involvement in this series, even in extensive invasive tumors involving the bladder, challenges the reported clinical estimates of spread of the disease. Bivens reported spread beyond the vagina in 42 of 46 cases. Kaiser found extension beyond the vagina in 31 of 55 cases. These findings cannot be questioned when involvement of bladder or rectal mucosa, bone, and vulva has occurred, but if spread is suspected from thickening of the rectovaginal septum or parametria, the likelihood of inflammatory induration should be kept in mind.

It is the personal opinion of the author that every patient with this disease should be considered as a candidate for radical surgery before radiation therapy is resorted to. Results from radiation treatment in a variety of clinics have not been encouraging, as Table I shows. In the opinion of Singh and Way (12) this result has been partly due to technical difficulties in the accurate application of radium in the vagina, and special instruments have been designed by Way (13), Focht, Marinelli, and Twombly to overcome such difficulties. Furthermore, as Way points out, there appears to be a wide variation in the radiosensitivity of vaginal carcinoma. Surgery has one great advantage in treatment: removal of the organ from which the tumor arises. The importance of this is apparent when one considers the frequency of recurrences or residual tumor in the vagina after radiation therapy or partial colpectomy.

If radical surgery is considered, it should be remembered that these procedures are formidable and must be individually planned with the aim of producing cure. Extensive operations with the removal of sphincters and diversion of the urinary stream cannot be justified when only a palliative result is in prospect. The age and condition of the patient should be carefully considered. Moreover, it is becoming increasingly apparent to those engaged in this type of surgery that the temperament of the patient is a large factor in the postoperative course and return to a useful and happy existence.

Fig. 12. Case 3. Penetration of a small subepithelial lymphatic channel by carcinoma cells. This was a surface tumor with minimal invasion. ×240.

The extent of surgery must be planned to fit the individual case. The finding of tumor beyond the clinically described limits in the vagina in half of these cases would seem to call for total removal of the vagina in every instance. It seems illogical to carry out extensive radical procedures, leaving behind a portion of the organ from which the tumor arises. In the experience of the author, total colpectomy is most accurately accomplished by a combined vaginal and abdominal dissection. When less than this is contemplated, extensive preoperative biopsies should be carried out to determine the lower limit of the lesion. At the time of the major procedure, this area should be defined by the application of clips or clamps vaginally, before the abdominal approach is begun. Removal of the uterus, adnexa, parametria and a block dissection of the pelvic lymph nodes are necessary for both therapeutic and prognostic reasons. In the advanced case extending into the lower third of the vagina, vulvectomy and dissection of

the inguinal nodes may be indicated as well. This course prolongs the operative procedure, however, and it has been the policy on this service to defer decision on inguinal node dissection until pathologic study of the excised pelvic nodes has been carried out. Removal of the bladder or rectum may be required when these structures are involved; but study of the specimens in this series indicates that the rectum may be uninvolved despite the presence of extensive tumor in the overlying vagina.

The number of cases in this series is far too small, and the observation of these patients obviously too brief, to permit a conclusive statement regarding the superiority of surgical treatment of carcinoma of the vagina. It is believed that pathologic observations from these specimens point clearly to the advantages of this approach, and it is hoped that similar studies will be carried out elsewhere to supplement our knowledge in this respect.

SUMMARY AND CONCLUSIONS

1. A study of the gross and microscopic pathology of surgical specimens from 8 cases of primary carcinoma of the vagina is presented.

2. Gross tumor forms are described which correspond to the clinical classification already in use. These are: everting tumors, infiltrating tumors, and surface tumors.

3. Microscopic studies showed a rough correlation of tumor architecture, differentiation, and mode of invasion to gross appearance. Everting tumors were generally well differentiated, papillomatous growths; infiltrating tumors were usually anaplastic and diffusely invasive; surface tumors were largely intraepithelial and moderately well differentiated.

4. Tumor spread beyond the vaginal limits described clinically was found in 4 of the 8 specimens.

5. No involvement of the parametrial or pelvic lymph nodes was found in the 6 cases in which these tissues were excised. In the remaining 2, survival indicates that these nodes were probably free of tumor.

6. Tumors of the posterior vaginal wall reached a considerable size and distended the vaginal muscularis without involvement of the rectovaginal septum or penetration of the rectal wall.

7. The extent of tumor found in these specimens indicates that present methods of clinical staging in this disease are unreliable.

8. Wider use of radical surgery in the treatment of this disease is recommended, and the reasons for this are discussed. It is urged that operation should include total rather than partial colpectomy.

9. It is hoped that careful study of surgical specimens of this disease will be carried out and reported in other institutions to provide information on this subject.

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ENZYMATIC DÉBRIDEMENT (STREPTOKINASE AND STREPTODORNASE) IN THE TREATMENT OF PELVIC ABSCESSES

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IN 1952, a preliminary report was published on the use of streptokinase and streptodornase in pelvic abscesses(1). The methods and results in 11 cases on the Tulane Gynecological Service at Charity Hospital in New Orleans in which streptokinase and streptodornase had been used as an integral part of the management of this condition were discussed in this paper.

It is our purpose in the present article to present the results in a greater number of similar cases and the follow-up studies on these patients to date, as well as a comparison of the valuation of treatment in a similar number of cases treated by the older and universally accepted method of management, described by Crossen.

The extensive reports in the literature on the use of streptokinase-streptodornase (SK-SD) in surgical conditions in which lysis of fibrin clots and the breakdown of fibers formed by desoxyribonucleoprotein in purulent exudates were so successful prompted us to investigate its use and efficiency in the treatment of cul-de-sac and tubo-ovarian abscesses that are directly accessible through the posterior fornix of the vagina.

On the Tulane Gynecological Service at Charity Hospital SK-SD has been used as a means of medical débridement in suppurating superficial wounds, incisional hematomas, cuff abscesses, and hematomas. The results have been generally good and compare favorably with those reported elsewhere in the literature regarding like conditions in other parts of the body.

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The results that we expected to obtain on the basis of our previous experience and those of many investigators in other fields of surgery and medicine were as follows: decrease in the viscosity of the purulent material; reduction of hospital days as compared to the older method; more complete evacuation with resultant decrease in recurrences and formation of adhesions; reduction of definitive surgery, such as hysterectomy and bilateral salpingo-oophorectomy. Since many of these patients fall in the age group of 20 to early 30, the later result, if obtained, would be a marked improvement over previous treatment.

The pharmacology of streptokinase and streptodornase has been reviewed frequently since the discovery of streptokinase by Tillett and Garner (5) in 1933 and Sherry's (4) discovery of the presence of desoxyribonuclease in the filtrate from certain strains of beta hemolytic streptococcus. Suffice to say then, that the streptokinase factor acts with the euglobulin factor in plasma to become an active fibrinolytic substance by inhibiting the change of fibrinogen to fibrin. Streptodornase acts to catalyze the breakdown of desoxyribonucleoprotein, which forms fibrin-like bands in purulent exudates, decreasing the viscosity of the purulent material. It is also definitely shown that the two substances do not attack healthy, living tissues. Therefore, the physiologic result would be an increase in the phagocytically active cells due to the removal of cellular debris and degenerated cells which would also bring about a greater diffusion by the general circulation of any medication or antibiotic that it might be carrying. This more thorough débridement would reduce the formation of dense fibrous adhesions that are

Fig. 1. Types of T tubes used in colpotomy—a comparison of size.

a basic cause of some of the invalidism following pelvic inflammatory disease with pelvic abscess formation and a fundamental background for sterility problems.

MATERIAL

The material for the substance of this report was obtained from two separate series of cases from the Tulane Gynecological Service of Charity Hospital at New Orleans. The first, including those in the preliminary report, was made up of 28 cases of pelvic abscess, 16 of which were cul-de-sac abscesses and 12 tubo-ovarian abscesses that presented an accessible mass in the cul-de-sac. In all of these cases colpotomy and the administration of SK-SD constituted the treatment used, and this group will be referred to as the SK-SD series. The races represented were white (1) and colored (27), and the age distribution was from 17 years to 63 years (Table I).

TABLE I.—TYPE OF ABSCESS AND AGE DISTRIBUTION IN SK-SD SERIES

	Cul-de-sac	Tubo-ovarian	Total
No. of cases	16	12	28
Race			
W	—	1	1
C	16	11	27
Age, years			
10–20	—	1	1
20–30	5	6	11
30–40	6	5	11
40–50	4	—	4
50–60	—	—	—
60–70	1	—	1

The second series used for comparison was made up of patients treated by the same methods except that SK-SD was not employed and the large 3 centimeter colpotomy tube was utilized. This group consisted of 28 patients, 14 with cul-de-sac abscesses and 14 with tubo-ovarian abscesses, and is retroconsecutive to July 1, 1951 when the SK-SD series was begun. This series included 4 white patients and 24 colored patients and their ages were distributed from the late teens to 64 years (Table II). This group will be referred to as the colpotomy without SK-SD series.

METHODS AND PROCEDURES

The methods and procedures were identical in both groups as to general medical and surgical management. All patients had colpotomy drainage and were given antibiotics, even in the presence of a negative culture. However, the SK-SD group differed in that these patients were given varidase into the abscess cavity following cul-de-sac puncture for diagnosis at the time of admission whether in the admitting room or the gynecologic clinic. In the gynecology department at Tulane cul-de-sac centesis has long been advocated as a diagnostic procedure, not only for suspected hemoperitoneum from whatever cause but also for the diagnosis of ruptured ovarian tumors, purulent peritonitis, pelvic abscess formation, and hematoma, since it is believed to be a rather benign procedure which can be done with equal ease in the doctor's office, the clinic, the ward, or operating room and which provides very important diagnostic information.

Varidase is a refined, dried SK-SD filtrate containing 100,000 units of streptokinase and 25,000 units of streptodornase that is diluted at the time of use with 10 to 20 cubic centimeters of normal saline solution. This solution was injected into the abscess cavity following the diagnostic cul-de-sac puncture. Approximately 5 to 30 cubic centimeters of

he exudate were withdrawn, depending on he size and tension of the mass, and 4 to 20 ubic centimeters of the varidase solution ere instilled through the same needle while was still in place. The amount of varidase lution injected was never larger than the nount of exudate removed. Approximately to 24 hours later the patient was taken to rgery and a colpotomy was performed, the culations were broken up digitally, and a 1 ntimeter gallbladder T tube was inserted in e cavity—an improvement upon the large 3 ntimeter rubber tube that was used previous July 1, 1951 (Fig. 1). The cavity was then stilled through the T tube with 1 ampule of ridase (100,000 and 25,000 units) dissolved 20 cubic centimeters of normal saline, daily, 4 days, after which the colpotomy tube was moved. It is believed that the patient lying the recumbent position without back rest ains the solution for a length of time necesy to allow the solution its maximum enzytic activity before it is discharged by dendent drainage. Miller and Long advised use of air-vent suction in treating perital infections but this procedure was not rried out in this series.

Viscosity studies were made in 8 consecutive patients. The method was discussed in the preliminary report where it was studied in 3 cases in that series (Fig. 2). The change in viscosity was measured before and after the introduction of varidase. The proof that the exudate became much less viscid was so positive that the measurement of the viscosity was discontinued after 8 cases. Only 1 exudate did not change and it was relatively thin before the introduction of varidase (Table III). All exudates in the remaining cases that were classified as thick changed in character and became more fluid and profuse.

RESULTS OF THE STUDY

When the two series were each divided into two groups according to the type of abscess, namely cul-de-sac abscesses (group I) and tubo-ovarian abscesses (group II), it was found that the average number of days spent in the hospital for the patients in group I who were treated with SK-SD was 9.25 and for the group who did not receive SK-SD was 15.08,

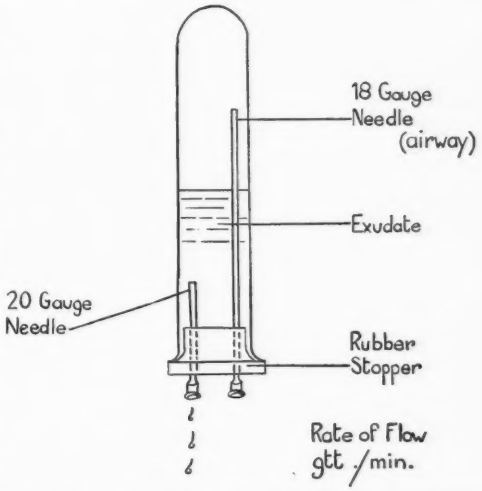

Fig. 2. Method used to test viscosity before and after varidase instillation.

or a difference of approximately 6 days (Table IV). The postoperative time was reduced from an average of 11.7 days to 4.6 days. As is known, the colpotomy tube comes out by itself frequently which accounts for the fact that the average time for the tube to be out in the SK-SD group was in only 3.7 days instead of the 4 days, as described in the method. The larger tube used in the patients without SK-SD came out in 7.9 days (average), and it was observed that when the larger tube fell out by itself the colpotomy had to be reopened and

TABLE II.—TYPE OF ABSCESS AND AGE DISTRIBUTION IN COLPOTOMY WITHOUT SK-SD SERIES

	Cul-de-sac	Tubo-ovarian	Total
No. of cases	14	14	28
Race			
W	1	3	4
C	13	11	24
Age, years			
10–20	—	3	3
20–30	7	7	14
30–40	5	3	8
40–50	1	1	2
50–60	—	—	—
60–70	1	—	1

TABLE III.—CHANGE IN RATE OF FLOW THROUGH 20 GAUGE NEEDLE AFTER VARIDASE INSTILLATION

Case No.	Rate of flow, gtt./min.	
	Before SK-SD	After SK-SD
1	0	36
2	0	16
3	4	8
4	4	16
5	23	23
6	9	18
7	0	24
8	17	22

the tube reinserted. The findings in group II followed the same pattern. Those who had injections of SK-SD spent a total (average) of 9.6 days in the hospital, the postoperative time was 5.7 days, and the T tube was out in 5.3 days. The group that did not receive SK-SD spent 15.3 days, or again about 6 days longer; there was an 11.7 day postcolpotomy period, and the larger tube came out in 8.8 days.

There was a great difference in morbidity in the two series. Using the accepted measure of 1 postoperative day with a temperature to 101 degrees or a postoperative elevation to 100.4 degrees for 2 days, the average number of morbid days was 1.1 for the series in which SK-SD was administered while for the control group the average was 5.4 days.

There was 1 death in the SK-SD series. This was in a 25 year old colored female who was admitted with pelvic peritonitis and a mass in the cul-de-sac from a tubo-ovarian abscess. She was treated in the same manner with colpotomy and varidase irrigations. The infection spread beyond the pelvis and extraperitoneal drainage was used. Two days later she complained of shortness of breath and chest pain, and she died in a few minutes from what was clinically diagnosed as pulmonary embolism.

TABLE IV.—COMPARISON OF HOSPITAL COURSE BETWEEN THE TWO SERIES

	Group I, 28 cases Cul-de-sac		Group II, 28 cases Tubo-ovarian		Total
	SK-SD	Without SK-SD	SK-SD	Without SK-SD	
No. cases	16	14	12	14	
Hospital days Total	9.25	15.08	9.6	15.3	
Postcol-potomy	4.6	11.7	5.7	11.7	
Morbidity	.6	5.3	1.7	5.5	
Day tube out	3.7	7.9	5.3	8.8	
Culture SK-SD Positive	5		6		11
Negative	11		6		17
Without SK-SD Positive		3		7	10
Negative		11		7	18

FOLLOW-UP STUDY

All patients who have returned to the clinic have been followed regularly and examined frequently with the purpose of evaluating the residual condition after the addition of SK-SD to the treatment. This follow-up study has continued until the present time, unless it was believed that the pelvis was normal in which case the patient was discharged. The time interval after colpotomy for patients in both series was from a minimum of 6 months to a maximum of 3 years.

Comparison of the two groups indicated that those patients who were treated with the aid of SK-SD evidenced less pain, fewer residual masses, less fixation of the uterine fundus and adnexa, a lesser number had to have definitive surgery at the time of hospitalization or later, and there were more individuals who were discharged with what was termed a clean pelvis. Two women became pregnant, one of whom had a tubo-ovarian abscess, and both delivered normal infants. Only 1 patient in the control series became pregnant (Table V). The 1 patient who is listed as having an acute flare-up on another service was found to have carcinoma of the cervix but no pelvic abscesses were present at the time of laparotomy. Two of the patients are now scheduled for definitive surgery because of large fibroids not because of the residual from the pelvic abscess.

CONCLUSIONS

On the Tulane Gynecological Service at Charity Hospital in New Orleans enzymatic

débridement by the use of SK-SD has been found to be an adjuvant to drainage in the treatment of pelvic abscesses since its use in 13 cul-de-sac and 12 tubo-ovarian abscesses presenting in the cul-de-sac. The action and results in this entity compare favorably with those reported in the literature on the use of SK-SD in other parts of the body for many different diagnoses.

The results are compared with those in a similar group of patients treated by the same methods and antibiotics with the exception of the use of SK-SD, and it is found that the group that had SK-SD injections at the time of centesis of the cul-de-sac and irrigation through the smaller 1 centimeter T tube following colpotomy responded with a more complete evacuation of the abscess in a shorter period of hospitalization. Thus the formation of excessive granulation tissue and adhesions was prevented and the uterus and adnexa were allowed to return to a more normal state in the pelvis which, in turn, obviated the need for definitive surgery. The action of SK-SD in reducing the barrier between the humoral and cellular elements, allowing the increase in phagocytosis and the accessibility of the specific antibiosis, has to this date reduced the recurrence of the disease by increasing the sterility of the tissue involved.

The scope of cul-de-sac puncture as a diagnostic aid has been increased by its use in any true cul-de-sac mass. Many condemn its indiscriminate use, but on the Tulane service it has yet to be seen as provoking any immediate or late complications when it was used as a true cul-de-sac diagnostic aid. Its value lies in the fact that it is a simple procedure which can be carried out in the examining room or the physician's office without anesthesia, and in the fact that it can be used as a procurer of material for the differential diagnosis of many pelvic conditions other than ectopic pregnancy.

It has been reported that SK-SD when injected into empyema cavities and other large abscess pockets caused an immediate thermal reaction. This reaction was not observed in our study, nor was any normal tissue affected by the SK-SD as far as could be observed. The fact that 2 patients in the group became pregnant and delivered normal infants substantiates this conclusion.

TABLE V.—EVALUATION OF END RESULTS OF THE TWO SERIES

Findings	Colpotomy and SK-SD		Colpotomy without SK-SD	
	Group I Cul-de-sac	Group II Tubo-ovarian	Group I Cul-de-sac	Group II Tubo-ovarian
Pain	1	1	3	7
Acute flare up	1	0	0	0
Menorrhagia	0	0	0	1
Mass	1	2	5	6
Fixation	2	0	6	7
Future surgery	3	0	2	2
Definitive surgery	1	0	2	4
Became pregnant	1	1	1	0
Died	0	1	0	0
Discharged	5	5	3	0
Did not return	3	1	1	1

SUMMARY

1. Streptokinase-streptodornase was used in the treatment of 28 patients with pelvic abscess.

2. The method and results of enzymatic débridement are described.

3. The results are compared with those in 28 cases of pelvic abscess in which SK-SD was not given.

4. SK-SD decreased the viscosity of the exudate in the 8 cases by actual measurements.

5. The 1 centimeter T tube was found adequate to provide complete drainage subsequent to colpotomy and irrigation with SK-SD.

6. The average hospital stay, morbidity, and duration of drainage were reduced in the SK-SD group.

7. The patients in the SK-SD series required less definitive surgery and demonstrated fewer symptoms and disease at clinical follow-up.

8. SK-SD is a safe preparation to use in the treatment of pelvic abscess.

9. Cul-de-sac puncture is a safe and excellent procedure to aid in the diagnosis of pelvic abscess.

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GUMMA OF THE BREAST

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THE two cases of gumma of the breast reported in this article are put on record for two reasons. The first is that the number of recorded cases is still small. At the most liberal count the total does not exceed 80, and the majority of these, as will be pointed out later, are of doubtful authenticity. The second reason is that because of the prompt and effective treatment of syphilis which is now the general rule, instances of this condition are likely to be encountered with increasing infrequency.

CASE REPORTS

CASE 1. A 46 year old negro woman was admitted to the Lutheran Hospital November 11, 1948, with a presumptive diagnosis of carcinoma of the left breast. She had first noticed a small mass in this breast, 5 months earlier, while bathing. At this time the mass was not painful. It gradually increased in size but did not become painful until 3 months before she entered the hospital. Then the overlying skin became ulcerated, the mass broke down, and a discharge appeared on the surface of the breast. The previous history was essentially negative except for a spontaneous abortion and the deaths of 2 children in early infancy.

The positive findings upon physical examination were confined to the left breast, in the upper outer quadrant of which was a circumscribed, fluctuant, lobulated, tender mass. The mass was fixed to the underlying skin and subcutaneous tissues but not to the chest wall. The tissue was very firm. The overlying skin was ulcerated and the adjacent skin had a definite pigskin (peau d'orange) appearance. The nipple was not retracted, and there were no palpable axillary or supraclavicular lymph nodes.

Roentgenograms of the chest were negative. Routine laboratory studies were also negative except for the Kahn serologic test, which was doubtfully positive, and the Mazzini test, which was positive.

The lesion had all the appearance of a typical fungating carcinoma. The chief of the surgical service, therefore, performed a radical left mastectomy on November 15, 1948, omitting preliminary excision of the tumor for biopsy, which is almost routine in this hospital. On gross examination the mass was found to be a sharply demarcated, lobulated, encapsulated nodule measuring 8 centimeters in diameter and consisting of moderately firm, grayish yellow tissue. Frozen section, carried out chiefly to satisfy our curiosity, showed inflammation and secondary infection. The tentative diagnosis of syphilis was confirmed 3 days later when completed studies showed the lesion to be a gumma. Histologic examination revealed an endarteritis obliterans, with a perivascular cuffing of lymphocytes, a varying degree of gummatous necrosis, and secondary inflammation (Fig. 1).

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The patient was returned to the referring physician for specific therapy. She has had no further difficulty referable to the breast.

CASE 2. A 20 year old negro woman was admitted to the Lutheran Hospital March 20, 1951, with a presumptive diagnosis of carcinoma of the left breast. The past history was noncontributory except for the breast lesion. According to the patient, her breasts began to develop when she was about 14 years old, and at about the same time she first noticed a small, painless mass in the left breast. This mass increased in size as the breasts became larger, but it had never been painful nor had there ever been a discharge from it or from the nipple. Four months before she entered the hospital she had given birth to a full term child whom she had nursed for about a month. The mass had not increased notably in size during her pregnancy but became considerably larger after delivery.

Physical examination was essentially negative except for the lesion in the left breast. This was a circumscribed, lobulated, freely movable, nontender nodule in the upper outer quadrant, extending from the nipple to the periphery of the breast proper. The nipple was not retracted and there were no palpable axillary or supraclavicular lymph nodes.

Roentgenograms of the chest were negative. Routine laboratory studies were also negative except that the Kahn serologic test was 4+ positive.

The nodule was excised by one of us (H.T.W.) March 23, 1951, on the diagnosis of fibroadenoma. Gross examination showed it to be an encapsulated, oval-shaped mass, measuring 9 by 7 by 6 centimeters. It was composed of individually lobulated nodules of firm, rubbery, grayish yellow tissue separated by varying amounts of stroma (Fig. 2). A rapid frozen section eliminated malignancy and resulted in a tentative diagnosis of inflammation, probably of syphilitic origin. The final pathologic report was gumma. Histologic examination revealed an endarteritis obliterans with perivascular cuffing of lymphocytes (Fig. 3) and varying degrees of gummatous necrosis (Fig. 4).

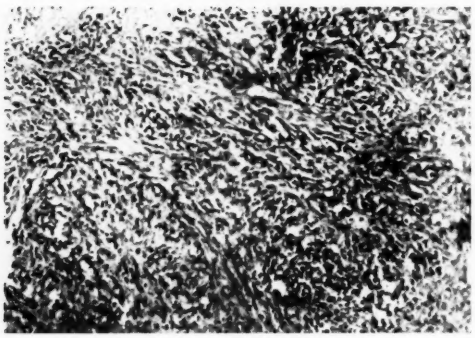

Fig. 1. Gummatous necrosis.

The patient was returned to the referring physician for specific treatment. It is known that she has had no further difficulty referable to the affected breast, but her present serologic reaction is unknown.

COMMENT

Recorded cases. The 2 cases of gumma of the breast reported in this communication were encountered in a total of 917 breast tissues examined in the pathologic laboratory at the Lutheran Hospital in Vicksburg over the 6¾ year period ending March 31, 1951. The single case reported by Adair was encountered in 1,674 carcinomas of the breast observed at the Memorial Hospital in New York. The number of years covered by these cases is not stated. The case reported by Kampmeier in 1947 was the only instance of gumma of the breast observed in 610 cases of late benign

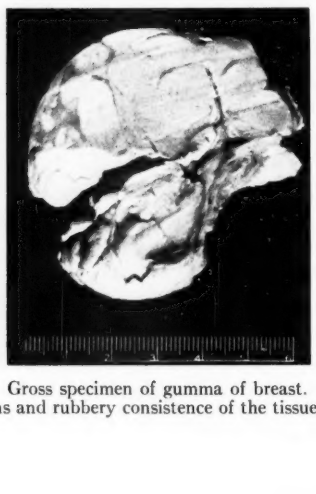

Fig. 2. Gross specimen of gumma of breast. Note the lobulations and rubbery consistence of the tissues.

syphilis treated at the Syphilis Clinic of Vanderbilt University Hospital over the previous 20 years. These figures clearly support Adair's statement that the rarity of this lesion is the explanation of why it is almost never recognized—most surgeons never see a case.

According to Adair, writing in 1924, 45 cases of gumma of the breast had been reported up to that time. To this number he added the case observed at Memorial Hospital in 1922. The first cases (2) were reported by Sauvages in 1768, but it was a hundred years later, Adair remarked, before the subject found its way into textbooks. Between 1768 and 1924, 29 additional observers reported 43 cases. In 1939, when he reported a personally observed case, Komori brought the number of recorded cases of gumma of the breast up to 75, including his own. The following year Braunstein and Woolsey reported an additional case, but the 5 cases which they collected from the literature are all included in the 28 cases collected by Komori after Adair's report. It is not clear whether the 2 cases reported by Hollosi in 1939 are the same as those mentioned by Komori in 1939 as having been reported in 1936. Hollosi mentioned in his 1939 article a case observed by Kleinschmidt, which is not included in the Komori collection. Counting all of these cases, the case recorded by Kampmeier in 1947, and the 2 cases which we are recording, the total number of cases of gùmma of the breast now on record in the literature does not exceed 82.

With few exceptions the articles on gumma of the breast concern single cases. In Adair's collection, 5 observers, like Sauvages, reported 2 cases each, another recorded 4, and still another recorded 5. In Komori's collection, 1 observer, Akaiwa, reported 11 cases and 1 reported 3 cases. It has already been pointed out that it is not clear whether Hollosi recorded 2 or 4 cases.

It would be naive to accept the 80 odd cases of gumma of the breast recorded in the literature as being even approximately correct. An examination of Adair's tabulated data shows omissions, deficiencies, and inconsistencies which make the validity of most of them highly doubtful. Adair himself pointed this out. In only 3 cases, including his own, was

a serologic study made. Its performance was considered in another case reported by Yvert in 1912, but the idea was given up on the ground that the test would cost too much. Histologic examination was carried out in only 4 cases, including Adair's own case. It was negative in 1 instance and positive in the other 3 instances. "Had it been more frequently made," wrote Adair, "we would have found more cancer cases in this series; and fewer gummata." The comment seems fair enough. Billroth doubted the diagnosis of gumma of the breast in 1 of the cases in which an autopsy was performed. One of the 4 patients reported by Landreau in 1874 was subjected to amputation of the breast and died later, after a spontaneous (pathologic?) fracture of the femur.

Histologic examination was carried out in the case reported by Komori but was omitted in some of the cases included in his collection in which the literature was available to us. For this reason neither of the cases reported by Hollosi in 1939 is conclusive. In the first case, the surgeon diagnosed the growth which he had removed from the breast of a 54 year old woman as carcinoma simplex. She was then sent to Hollosi, who found her Wassermann reaction 4+ positive. The other patient was treated by deep x-ray therapy under which the growth increased in size. She was also found to have a 4+ Wassermann reaction.

As these remarks show, not more than a dozen, at most, of the recorded cases can be accepted as confirmed gummas of the breast if the final diagnosis rests, as we think it should, upon the histologic examination. A positive serologic test is useful evidence, but the association of carcinoma of the breast and syphilis must be fairly frequent by the law of averages, and to assume that a breast tumor is a gumma merely because the serologic reaction is positive would seem a decidedly dangerous course of action.

The race, unfortunately, is not tabulated in Adair's series, presumably because it was not mentioned in most of the reports. Both of our patients were negroes. Kampmeier's patient and Braunstein and Woolsey's patient were also negro women.

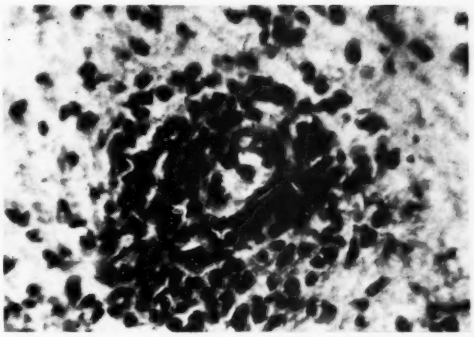

Fig. 3. Endarteritis obliterans with perivascular cuffing of lymphocytes and plasma cells.

In Adair's collected series the age, in the 33 cases in which it was stated, ranged from under 10 to 62 years. Three patients, like 1 of our own, were 20 years of age or under. In the 35 cases in which the sex was stated there were 3 men and 32 women.

Diagnosis. Theoretically, the clinical diagnosis of gumma of the breast should not be too difficult if the history, physical findings, and serologic studies were correctly evaluated, but the recorded cases suggest the contrary. In the 15 cases collected by Adair in which a preoperative diagnosis was made or in which a diagnosis was recorded before the progress of the condition clarified the diagnosis, 14 were diagnosed as carcinoma. In the single case in which the lesion was thought to be nonmalignant, no additional details were furnished. Many of the lesions, as in our first case, were

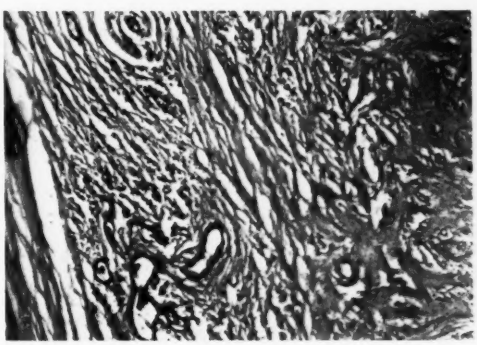

Fig. 4. Gummatous necrosis.

of stony hardness. Thirteen patients either had ulcerated lesions when they were first seen, also as in our first case, or their lesions went on to ulceration while they were under observation. In a number of the cases collected by Adair, as in our first case, surgery included not only amputation of the breast but excision of the axillary contents. His patient was saved from radical surgery because she did not appear for operation at the time specified. When she returned, the appearance of the lesion had so altered that he suspected some unusual form of infection. Incision produced dirty, liquefied necrotic tissue, unlike pus, and biopsy was performed. At this point the services of an interpreter were secured and questioning revealed a history of abortion and of syphilis in the patient's husband. Our first patient, incidentally, had a typical history of miscarriage and children dead in infancy but its significance was not appreciated until after operation. Kampmeier's patient was also saved from operation by her failure to reappear at the scheduled time. When she returned 5 weeks later, the lesion had broken down and gumma was suspected. In Kleinschmidt's case, cited by Hollosi, the diagnosis was carcinoma and operation, presumably, would have been performed had he not noticed the sunken appearance of the root of the nose which led him to suspect that the lesion was gumma. It disappeared under specific therapy.

The second of our cases, in spite of the long duration of the mass (6 to 7 years) still represents the first stage of Adair's six stages in the development of mammary gumma. The patient was a young woman and her lesion was a painless, circumscribed, freely movable nodule, without involvement of the skin. The diagnosis of a benign fibroepithelial tumor seemed reasonable and excision was performed on that basis.

Our first case falls into the fifth stage described by Adair. The patient who was 46 years of age presented a tender, irregularly lobulated mass, with involvement of the subcutaneous tissues and skin, superficial ulceration, and drainage of necrotic secondarily infected material. The lesion so closely resembled late carcinoma of the breast, as it is all too frequently seen, that an experienced surgeon performed a radical mastectomy without bothering to precede it by biopsy. It is somewhat embarassing to recall Adair's statement that the chief difficulties in the differential diagnosis of carcinoma and gumma of the breast occur in the first three to four stages and thereafter it is "simpler." In the light of this case we are not inclined to agree with him.

The differential diagnosis lies chiefly between tuberculosis and carcinoma. In cases of gumma, the loss of structure is likely to be less complete than in the caseation necrosis of tuberculosis. According to Kampmeier, whose experience of syphilis is extensive, ulceration of the skin occurs much earlier in gumma than in carcinoma, while tuberculosis is more likely to be associated with sinus formation than with the simple ulceration of the skin observed in gumma.

Pathologic process. Diagnosis in both of these cases was made, as we believe that it should be, according to the criteria long taught by Neal at the University of Missouri.

The characteristics of gummatous necrosis are not adequately described in most textbooks of pathology. According to Neal it results from the gradual cutting off, over a long period of time, of the arterial blood supply by an endarteritis obliterans (Fig. 3). The picture is similar to that of a coagulation necrosis, caused by the sudden occlusion of the arterial flow, as in embolism and infarction. The result is destruction of all tissues and structures except the blood vessels and surrounding strands of connective tissue. The appearance, according to Neal, suggests that of a town destroyed by a hurricane, where only paved streets and exposed water pipes remain visible among the wrecked and shattered buildings.

Grossly the gumma is an irregularly shaped lesion with indented margins. It is usually grayish white but may be yellow if fatty infiltration or degeneration has occurred and its consistency is dry and rubbery. It cannot be squeezed out or scraped away from the surrounding tissues, as is usually possible in caseation necrosis. In this respect it resembles an area of infarction.

Microscopically the gumma is characterized by varying degrees of coagulation necrosis, with occasional islands of living parenchymatous tissue, in which arterioles with intact endothelial linings may still be present. These vessels may show a perivascular cuffing of lymphocytes (Figs. 3 and 4). The necrotic and necrosing tissues can be recognized by their shadowy outlines. Lymphocytes, plasma cells, and endothelial leucocytes, as well as an occasional multinucleated giant cell, may be seen in the peripheral zones.

SUMMARY

Two additional cases of gumma of the breast, both confirmed histologically, are reported. Most of the approximately 80 cases recorded to date are not thus confirmed and are of doubtful validity. The pathologic process, details of which are lacking in most textbooks of pathology, is described. Biopsy is indicated in all cases before specific treatment is begun in order to exclude carcinoma; the differential diagnosis is not otherwise possible.

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CHRONIC ULCERATIVE COLITIS—ANORECTAL COMPLICATIONS

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AMONG the more devastating aspects of chronic ulcerative colitis are the inflammatory and malignant complications which occur in the anorectal region in about 15 to 20 per cent of patients. Unless these complications are handled judiciously they may lead to much more serious consequences such as anal incontinence necessitating ileostomy or in the case of an untreated polyp to a malignant lesion. In dealing with these complications most writers on the subject, including the authors, have advocated conservatism. In January, 1940, Smith and one of us (Jackman) stated that "indications for surgical interference in the treatment of anal conditions complicating or coexisting with chronic ulcerative colitis should be limited to emergencies." Since then, having repeatedly seen the consequences caused by frequently recurring abscesses in the anorectal area, we have changed our attitude somewhat. In cases of anorectal abscess, if one is so conservative as to limit surgical intervention to incision and drainage, an initial relatively simple fistula may progress to one much more complicated such as a rectovaginal fistula, or to a chronic inflammatory process of destruction of tissue and fibrosis causing anal incontinence. Many patients with frequently recurring anorectal abscesses who have never undergone any surgical intervention other than incision and drainage of abscesses are completely incontinent because of the destruction of muscle and immobilization of muscle by fibrosis. Others handled in the same manner may develop anorectal strictures necessitating ileostomy.

The anorectal complications of chronic ulcerative colitis are, in the order of frequency with which they occur: (1) polyposis and malignancy, (2) rectal stricture, (3) anorectal abscess and fistula, (4) hemorrhoids, (5) anal fissure and anal ulcers, and (6) anal incontinence.

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POLYPOSIS AND MALIGNANCY

Polyposis occurs in about 10 to 12 per cent of patients who have chronic ulcerative colitis. Bargen reported an incidence of 8.9 per cent in 1,500 patients. Since chronic ulcerative colitis usually begins in the rectum, it, therefore, is the commonest site of origin of polyps.

Early in their formation polyps are actually mucosal tags or pseudopolyps which may later become adenomatous or adenocarcinomatous. The mechanism of their formation is that in a destructive phase of the disease large areas of mucous membrane and submucosa will slough leaving large ulcers in the center of which may be an island or islands of inflammatory mucosa. As healing takes place, the island of mucosa, which is now surrounded by scar tissue, becomes reddened and edematous, rising up above the lèvel of the adjacent wall of the bowel, and grossly appears polypoid. Essentially the polyps occur as a result of nature's attempt at healing as destruction takes place.

Polypoidosis should be considered a serious complication of chronic ulcerative colitis because of the eventual adenomatous changes or true polyposis following which it may progress to malignancy. About 2 or 3 per cent of patients having chronic ulcerative colitis eventually develop carcinoma of the colon.

In the treatment of the polyps the progress of the disease should be observed clinically, by sigmoidoscopy and by roentgenologic examination, and a propitious time should be selected for fulguration of those polyps within reach of the sigmoidoscope. The ideal time for this is during a period of remission, keep-

ing in mind that fulguration may cause a temporary flare-up of the colitis. Polyps beyond reach of the sigmoidoscope should be checked at intervals for evidence of growth to adenocarcinoma in which event ileostomy and colectomy would have to be performed.

RECTAL STRICTURE

Rectal stricture is considered to be the second commonest complication in chronic ulcerative colitis. Narrowing of the lumen of the large intestine is the rule rather than the exception after two or three attacks of the disease. What we have particular reference to is localized areas of stricturing. These may occur at any place in the large intestine but are by far the commonest in the rectum. As to frequency, stricture was observed in 78 (9 per cent) of 871 cases reviewed. The stricture is due to scar formation resulting from an attempt at healing. Local treatment is not very satisfactory. If the chronic ulcerative colitis is quiescent a low-lying stricture may be treated by a posterior proctotomy, the mucous membrane above it being pulled down over the resulting wound. This procedure followed by hot retention enemas twice daily or rectal diathermy daily over a period of 6 to 8 weeks has proved satisfactory in some instances and has obviated the necessity of an ileostomy.

ANORECTAL ABSCESS AND FISTULA

Anal abscess or fistula is certainly one of the more serious complications of chronic ulcerative colitis. It ranked third in frequency of complications, being preceded by polyposis and stricture. In a study of 871 patients that Smith and one of us made in 1940, it occurred in 73 patients (8.4 per cent). It is most difficult to exercise proper judgment in the handling of this complication. Overconservatism on the one hand, with frequently recurring abscesses and destruction of tissue, may result in anal incontinence or anorectal stricturing and possible ileostomy. On the other hand, an attempt to eliminate the fistula by surgical intervention may result in an unhealed, indolent wound which may persist for years and cause great disability. In regard to surgical intervention a few definite statements can be made: (1) During an active phase of the disease, conservatism is desirable and surgical treatment should be limited to incision and drainage of acute abscesses. (2) During remissions of the disease it may be good judgment to perform fistulectomy in certain selected cases. Healing of the resulting wounds may be slow and if an exacerbation of the disease occurs the fistulectomy scar may break down, producing an indolent ulcer. Healing of the wound may be promoted by the use of roentgen therapy, or ultraviolet radiation—but particularly by making sure that there is adequate drainage. Overhanging edges and excess granulations should be removed as indicated when they occur.

HEMORRHOIDS

Whether hemorrhoids should be considered as a complication of chronic ulcerative colitis or a coincidental occurrence is beside the point. The two conditions frequently coexist and the main reason for discussing the question here is that many patients who have early chronic ulcerative colitis are unwittingly operated upon for hemorrhoids, much to the distress of the surgeon when he discovers that symptoms of bleeding persist after the operation. This, of course, further emphasizes the importance of proctoscopy before doing any anal operation. In the study that Smith and one of us (Jackman) made, 3.7 per cent of the 871 patients who had chronic ulcerative colitis stated that their symptoms of bleeding and rectal discharges were noticed shortly before, or at least symptoms became more pronounced after, the hemorrhoid operation. It should be borne in mind that diarrhea is not necessarily always a symptom of chronic ulcerative colitis. Actually, some patients in whom the disease is in an early stage, or at least confined to the distal rectal mucosa, may complain of constipation and it is this group which may be unwittingly operated upon for hemorrhoids.

ANAL FISSURE AND ANAL ULCERS

Painful anal lesions such as anal fissure and anal ulcers occur in about 5 per cent of patients who have chronic ulcerative colitis. Here again it is certainly best to avoid surgi-

cal intervention during an active phase of chronic ulcerative colitis. It is preferable to resort to palliative procedures. Measures which may be effective in relieving pain are the use of topical anesthetic ointments or suppositories. If the latter are used the patient should be instructed how to use them. It should be kept in mind that the pain caused by an anal fissure will cause a great deal of anal spasm and the suppository will either be pushed up into the rectum beyond the source of the pain or extruded to the outside. Therefore, the patient should be shown how to insert just the tip of the suppository into the anal canal, holding it in place with a piece of gauze until it starts to melt and then pushing it on into the anus. Another effective procedure in relieving pain due to anal fissue or anal ulcer is the use of hot anal irrigations. This procedure is rather simply done by filling the enema bag with plain hot tap water. The water should be as hot as the hand will tolerate it for a minute. The black plastic or hard rubber enema tip is replaced by a No. 18 F catheter. The enema outfit is hung on the wall adjacent to the toilet seat. After each bowel evacuation and while still seated on the commode the patient is instructed to lubricate the catheter and insert it into the anal canal for 1 or 2 centimeters, releasing the clamp and using the slow hot irrigation to wash out the infected secretions in the ulcers and relieve the muscle spasm. This procedure will require about 5 minutes. On some occasions such a procedure will promote healing of an indolent ulcer. Not uncommonly nature will heal a fissure by producing an abscess beneath its overhanging edge or "sentinel pile," with rupture of the abscess and the consequent production of a subcutaneous fistula. The fissure can then drain and healing will take place. In some instances it may be the part of good judgment to remove the sentinel pile or overhanging edge by infiltrating it with a local anesthetic and excising it. In this way the fissure can drain and healing takes place. Here again radical excision of the fissure or ulcer should be done only when the colitis is inactive.

ANAL INCONTINENCE

It is a frequent assumption that all patients with chronic ulcerative colitis who have anal muscle incontinence are in this predicament because of an unwarranted anal operation such as a fistulectomy. This is not necessarily true. Many patients who have never had any anorectal operation are completely incontinent because of general debility and weakness attendant on the disease while many others will have had so much destruction and scarring of anal musculature by repeated abscesses that any muscle action is completely absent. Most patients who have anal incontinence and an active chronic ulcerative colitis are better off with an ileostomy and a colectomy.

COMMENT

The attitude of complete conservatism in dealing with the rectal complications of chronic ulcerative colitis should be tempered with sound judgment.

Polypoid disease may eventually lead to a malignant lesion and, therefore, at a propitious time the polyps should be destroyed by fulguration or possibly by excision.

Anorectal strictures may sometimes be prevented by doing necessary fistula surgery at the proper time, that is, during a remission of the disease.

An active phase of the disease is usually a contraindication to any surgery other than emergency.

Symptoms from an early chronic ulcerative colitis and hemorrhoids may be very similar, and thus result in an unwarranted hemorrhoidectomy which may aggravate the colitis.

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ECTOPIC PREGNANCY

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DURING the past 6 years there have been several reports from Charity Hospital of Louisiana in New Orleans concerning ectopic pregnancy. Each report has emphasized several important factors concerning the incidence, diagnosis, treatment, and mortality. The first by Beacham and associates concerned 1,059 proved cases of ectopic pregnancy seen during the years 1906 to 1937. This covered the period before establishment of a residency system, sulfonamides and antibiotics, plasma or a blood bank. The mortality rate during this period fluctuated between 11.4 and 12.3 per cent. During the 10 year period beginning 1937 there was a drop in mortality to 2.8 per cent. This drop was due to the establishment of a residency system, better preoperative and postoperative care, and the advent of sulfonamides and antibiotics.

Collins' report in 1951 covered the period 1946 to 1951 and included a survey of 320 cases of proved ectopic pregnancy admitted to Charity Hospital. The mortality rate for this group was 2.2 per cent.

In the present report we shall cover the period January 1, 1951 to July 1, 1953, there being a total of 254 proved cases admitted to the hospital during that time. Of these, 133 were handled on the Tulane Unit at Charity Hospital. This report shows a continued increase in the number of ectopic pregnancies seen at Charity Hospital. We believe that this is due, not to an increase in hospital admissions, but actually to an increase in the number of such cases. How can such an increase be accounted for? With the advent of the sulfonamides and antibiotics, it was hoped that acute pelvic infections and their sequelae would be prevented or well controlled. This, however, has not taken place. The number of extensive tubo-ovarian abscesses, for instance, has shown little decrease as reported by the senior author. That report concerned 93 such patients admitted to the Tulane Unit of the Charity Hospital over a 5 year period, 1946 to 1951.

We believe that the use of the sulfonamides and antibiotics for acute salpingitis has been responsible in part for the increase in the number of ectopic pregnancies. Before these drugs were available, many of the patients would have developed complete occlusion of the tubes. At the present time these infections in the tubes are controlled before complete occlusion occurs. Fertility remains but because of intratubal or peritoneal adhesions, progress of the fertilized ovum is impeded and tubal implantation results.

We also believe that the time factor in beginning treatment of acute salpingitis is most important. Antibiotic therapy must be started before suppuration has occurred, this usually taking place about the fifth to seventh day of the acute process. Unless the treatment is begun before this time, tubal closure is almost certain to occur.

There is seldom a textbook picture of ectopic pregnancy. When a patient is admitted in shock and a history is obtained from a relative of 1 to 2 months' amenorrhea, sudden onset of pain, with vaginal bleeding and syncope, the diagnosis should be quite obvious and could be made by a third year medical student. We believe that diagnosis in the average patient who presents none of these signs or symptoms can be made only when such a condition is constantly kept in mind. On the Tulane service, the residents are taught to be ectopic pregnancy conscious. This fact perhaps can help explain the definite increase in the number of proved ectopic pregnancies during the period covered in this report which we have

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Fig. 1. Culdocentesis.

shown to be equal to the number that occurred during the previous 5 year period, 1946 to 1951.

A thorough history and physical examination are naturally of considerable importance. In many cases of ectopic pregnancy, an accurate diagnosis can at times be made on the basis of the history; such as disturbance in menstruation with or without abdominal pain and syncope. Many of our patients exhibited the usual symptoms of pain and bleeding. Approximately 65 per cent complained of some abdominal pain, and about 20 per cent complained of vaginal bleeding. These complaints alone or in combination with others seen less frequently are certainly insufficient for an accurate preoperative diagnosis of ectopic pregnancy. Such a presumptive diagnosis when made, however, should be confirmed by culde-sac puncture. This important diagnostic procedure will be discussed in greater detail later. Pelvic examination does not necessarily have to indicate pregnancy. However, in the presence of an adnexal mass with or without concomitant physical signs of pregnancy, ectopic pregnancy must always be considered. Bilateral ectopic pregnancy has occurred on 1 occasion at Charity Hospital of Louisiana in New Orleans in 1952.

The diagnostic procedure that we have found to be essential is culdocentesis. Other diagnostic procedures are time-consuming which fact, we believe, contraindicates their use in the average case, as we are dealing with a surgical emergency. We have found that knowledge of the contents of the cul-de-sac has been the key to an accurate diagnosis of ectopic pregnancy. Our experience has shown, that when properly done, culdocentesis has resulted in no known complications. Culdocentesis is a procedure that can be performed in the office, clinic, home, admitting room or hospital ward. Figure 1 shows the technique of this procedure.

Simply stated, culdocentesis is the introduction of an 18 gauge spinal type needle through the posterior vaginal fornix into the cul-de-sac and withdrawal or aspiration of its contents by means of a 50 cubic centimeter aspirating syringe.

The contents of the cul-de-sac may be divided into three categories: (1) clear straw colored peritoneal fluid, (2) frank unclotted blood, (3) a mixture of 1 and 2.

Clear straw colored peritoneal fluid may be found in the presence of an unruptured ectopic pregnancy, particularly in the presence of a unilateral adnexal mass. Such a patient is advised of this possibility and instructed to return to the hospital immediately if abdominal pain or abnormal vaginal bleeding occurs. Frank blood that does not clot within 10 minutes strongly indicates the presence of ectopic pregnancy. Pinkish fluid usually consists of several drops of blood mixed with peritoneal fluid, due to perforation of the vaginal mucosa, and may be considered as negative for ectopic pregnancy. Dark blood-colored peritoneal fluid must be evaluated on the basis of additional clinical factors and one's clinical experience. In most instances, however, this finding indicates an ectopic pregnancy. When no fluid is recovered from the cul-de-sac, the procedure is repeated. Two such aspirations on our service are considered as negative for ectopic pregnancy. However, if the examiner is still suspicious of its possibility, the patient is advised of such and instructed to return to the hospital immediately if abdominal pain or abnormal vaginal bleeding occurs. If this course is not practical, such patients are hospitalized for at least 24 hours for additional cul-de-sac study.

This report indicates our feeling regarding the diagnosis of ectopic pregnancy, the primary consideration being that the condition be constantly kept in mind, particularly during the child-bearing age. The second important factor is the determination of the cul-de-sac contents in such a patient. Recovery of pus on aspiration obviously indicates cul-de-sac or tubo-ovarian abscess, or occasionally a ruptured appendix. Greasy or cheesy material or yellow fluid that congeals on cooling is often found in the presence of a dermoid cyst of the ovary.

When the diagnosis of ectopic pregnancy has been established, operation is indicated immediately. At this time infusion is started, even if it requires a cut down. The patient is typed and cross matched and Rh factor is determined. Hematocrit determination is also done. If needed, blood is administered immediately. Nasal oxygen is given when needed. We wish to emphasize, however, that in no instance is surgery delayed for the patient to come out of shock or the hematocrit to be brought to normal by transfusion. Such patients can survive only if the bleeding point or points are controlled as soon as possible and the blood loss is replaced immediately. We wish to re-emphasize at this time that no surgical procedure should be performed except that which is necessary to control bleeding, unless the patient is found to be in excellent condition.

In the average case, general anesthesia is the agent of choice. This consists of ethylene and ether. We are opposed to the use of cyclopropane because of its effect on blood pressure. In a small group, where indicated, local anesthesia is used. Rarely, due to extreme urgency or deep shock, we have operated without anesthesia, using oxygen only. Following this regimen on the Tulane service since January 1951, 133 consecutive cases of proved ectopic pregnancy have been handled through the abdominal approach without the occurrence of a single fatality.

Figure 2 shows the mortality changes from 1908 to the present time. There has been a steady decrease in the mortality from ectopic pregnancy at Charity Hospital of Louisiana in New Orleans since 1908. During the period

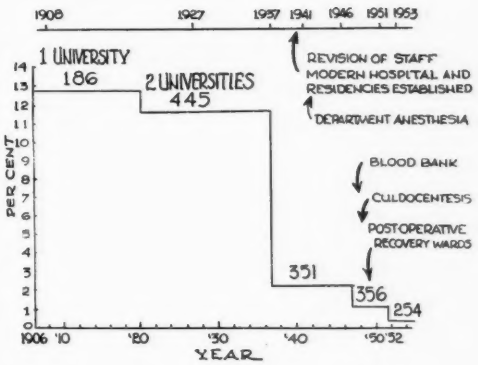

Fig. 2. Mortality rate uncorrected.

1908 to 1920 the rate was 12.3 per cent. From 1920 to 1937 the mortality rate was 11.4 per cent. During the period 1937 to 1946 the rate fell precipitously to 2.7 per cent. In the period 1946 to 1951 this low rate continued, being 2.2 per cent. From January 1951 to July 1953, the period covered in this report, the rate dropped again to .38 per cent. The 1 death occurred in the admitting room July 22, 1951 before diagnosis could be made. The patient was then admitted to the hospital administratively for the purpose of performing an autopsy which revealed a ruptured ectopic pregnancy as the cause of death.

CONCLUSIONS

1. There is no doubt that the incidence of ectopic pregnancy at Charity Hospital of Louisiana in New Orleans is increasing.

2. We believe that this increase is probably due to two factors, the first being the wide use of antibiotics and sulfonamides in the treatment of acute salpingitis. Such drugs apparently prevent complete tubal closure or occlusion. Secondly, is the fact that our residents are ectopic pregnancy minded and are diagnosing more cases correctly.

3. Culdocentesis is the key to accurate diagnosis since this procedure clearly indicates the contents of the cul-de-sac.

4. The management of ectopic pregnancy consists of immediate operation without procrastination, irrespective of the patient's condition.

5. Surgery should be limited to that necessary to control intra-abdominal bleeding, unless the patient is in excellent condition.

6. The use of blood for adequate replacement cannot be overemphasized.

7. The anesthetic of choice is ethylene and ether.

8. The mortality under this regimen has continued to decrease, 254 consecutive cases of proved ectopic pregnancy having been managed at Charity Hospital of Louisiana in New Orleans during the period January 1, 1951 to July 1, 1953 without fatality.

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A MODIFICATION OF THE DYE-DILUTION METHOD FOR SERIAL ESTIMATIONS OF PLASMA VOLUME

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THE recent upsurge of ultraradical surgery places considerable emphasis upon the availability of large amounts of blood and the liberal use of blood transfusions. Such massive blood transfusions require a reasonable control in their administration by balancing the losses with replacement and, because of the impossibility of estimating the amount lost with sufficient accuracy, over or under transfusions are not too infrequent. Such accidents could be prevented if a method were available which would permit a continuous determination of the volume of circulating blood in order to permit the surgeon or anesthesiologist to make the necessary adjustments, and thus maintain the blood volume at optimal levels.

Such an ideal method has not, as yet, been devised, but the present report relates to a modification of an accepted method for repetitive blood volume determinations, which might prove to be a useful, although temporary, solution to the problem.

The simplest and probably the most reliable method for the determination of plasma volume is the dye dilution method using T-1824 (Evans blue), the clinical application of which has been studied in great detail. The amount of dye ordinarily employed for each determination produces a discoloration of the patient's skin, which, if repeated once or twice will reach such intensity that it may become objectionable. If such determinations are repeated on the same patient as a life-saving procedure such effects are of secondary importance, but most of the time they are not performed for such reasons.

Nevertheless, it is frequently desirable to obtain checks by performing duplicate determinations, since a clinical test or procedure of this type is subject to numerous errors. While the laboratory procedures can be performed with almost any degree of precision and accuracy, errors in the administration of the dye, the sampling of blood, and its collection after specific time intervals may lead to mistakes in the routine application of the method.

The present study was undertaken to investigate the possibility of reducing the amount of dye to be used for each test, to determine the lower limit of the quantity of dye which can be used for clinical purposes, to study a number of possible simplifications of the procedure, to devise a routine for serial blood volume determinations, and finally to illustrate the applicability of this modification by means of several examples.

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METHODS AND MATERIALS

Three different solutions of dye were employed in these investigations. The first of these, hereafter referred to as the "stock solution," was a commercial product of Evans blue (T-1824) which had been prepared in a concentration of about 0.3 per cent. This material is available in 5 cubic centimeter sterile vials and is suitable for intravenous administration.

The test solutions employed during the present investigations were considerably more dilute, a necessary circumstance for the accurate administration of the dye. These test solutions were prepared by adding 5 cubic centimeters of the stock solution to 20 or 30 cubic centimeters of normal saline. Since an accurate dilution under sterile conditions was considered dangerous if a routine application were contemplated, the concentration of dye in the test solution had to be determined for each batch.

This analysis then leads to the preparation of the third solution already mentioned. Only a fraction of the test solution, the concentra-

tion of which ranged from 0.04 to 0.06 per cent, was used for the estimation of plasma volume, and an aliquot was set aside for an accurate analysis of its dye content. This was accomplished by a volumetric dilution in the ratio of 1:250 or 2:250 using normal saline as solvent and reading the color intensity against pure water or saline.

The determination of the optical density by means of a Beckman spectrophotometer (model DU), using corex or quartz cells, constituted the main analytic procedure. For all routine determinations an arbitrarily chosen wave length of 620 millimicrons was used although the absorption maximum for T-1824 in saline or water is known to be somewhat lower. Since the readings on the aqueous solutions and plasma samples were usually done at about the same time, a reading at a constant wave length appeared to be more practical. This course necessitated the preparation of two standardization curves: one indicating the dependence of optical density on dye concentration in water or saline, and the other relating to the same solute in plasma.

The administration of the dye. Although the simplicity of the standard procedure leaves little to be desired, the method of administration of the dye is inaccurate. In order to transfer 3 to 5 cubic centimeters of a concentrated dye solution quantitatively into the vascular system of a subject, elaborate precautions are necessary. Thus, the dispensing syringe would have to be weighed before and after the administration of the dye, or the dye remaining on the barrel and plunger would have to be collected by rinsing and determined separately. These and similar adjustments, which are outlined in detail in the physiologic literature dealing with this subject, are too cumbersome for routine clinical application. They can be avoided by the use of the arrangement to be described.

A schematic presentation of the setup used throughout our experiments is given in Figure 1. All individual parts, with the exception of the volumetric burette, are available commercially or can be obtained from the stock rooms of any general hospital.

The glass stopcock of a standard 25 or 50 cubic centimeter volumetric burette was cut off and the tip tapered or ground to fit a standard hypodermic needle. The burette was washed with cleaning solution, carefully rinsed, and autoclaved in the usual manner. The burette should be absolutely dry before use, and for this reason autoclaving seemed to be preferable to sterilization by boiling. The rubber protection over the dispensing cap of a secondary venopak (list No. 4113) was torn off, the air filter discarded, and the tip of the burette inserted into the hole leading to the plastic tubing. A 22 or 24 gauge hypodermic needle placed over its tapered end was protected from contamination until ready for use. The diluted dye was then transferred into the burette and the whole system filled to the tip of the needle. A Hoffman clamp, placed anywhere along the plastic tubing, served to regulate or check the flow of dye. The use of such a clamp is preferable to a 2 or 3 way stopcock.

An infusion of isotonic saline was started on the patient and allowed to continue for a few minutes in order to check the system for leaks. The infusion was stopped by means of another clamp placed high up on the plastic tubing leading to the infusion bottle. The system containing the dye was then connected with the infusion by inserting the needle (filled to its tip) into the plastic infusion tubing. The Hoffman clamp on the plastic tubing leading to the burette was opened and a known amount of the diluted dye allowed to flow into the infusion system. The clamp was closed tightly and the dye trapped in the infusion system washed into the circulatory system of the patient by opening the clamp on the plastic tubing leading to the infusion bottle. The washing was usually found to be complete within 60 to 90 seconds and was stopped as soon as the solution in the lower portion of the tube had lost its blue tinge which, incidentally, represents an excellent index of the completeness of the transfer.

After 10 to 12 minutes were allowed for adequate mixing, a sample of blood was withdrawn from the opposite arm, or, during operations, from a major abdominal vessel, and another administration of the dye was initiated in the manner which has already been described.

DETERMINATIONS OF DYE IN PLASMA

For an estimation of the concentration of the dye in plasma, blood was withdrawn without stasis and collected in large (6.00 c.c.) hematocrit tubes containing approximately 0.7 milligram of powdered heparin. The tubes were then centrifuged at 3,000 revolutions per minute for 15 minutes and the hematocrit noted. An aliquot of plasma was then transferred to 1 or 3 cubic centimeter corex cells, and the color intensity at 620 millimicrons determined by means of a Beckman spectrophotometer. It was read against a sample of plasma obtained before administration of the dye.

CALCULATION OF RESULTS

For the calculation of results any arbitrarily chosen unit will serve the purpose if its use is consistent. The units employed can refer to milligrams of dye, cubic centimeters of stock solution, or cubic centimeters of the particular test solution employed. It was found most convenient to use the stock solution as the primary standard and to express the data needed for the calculations in terms of cubic centimeters of stock solution.

The freshly prepared test solution, in spite of its relatively high dilution, is too concentrated for reliable readings on the spectrophotometer. A quantitative dilution of 1:250 or 2:250 brings it into the most favorable range of the instrument. The concentration of dye in the test solution expressed in cubic centimeters of stock solution is then calculated from the ratio x (250/a) where 250/a represents the dilution ratio and x the concentration estimated from the calibration curve.

The volume of test solution infused is then multiplied by this factor in order to calculate the total units (c. c. of stock solution) administered. If the concentration of dye in plasma in the same units is known, the volume of plasma can be derived from the ratio:

$$\text{Plasma volume} = \frac{\text{Amount of dye injected}}{\text{Concentration of dye/cubic centimeters of plasma}}$$

The total blood volume is then calculated according to the familiar equation:

$$\text{Total blood volume} = \frac{100 \text{ Plasma volume}}{100 - 0.96 \text{ Hematocrit}}$$

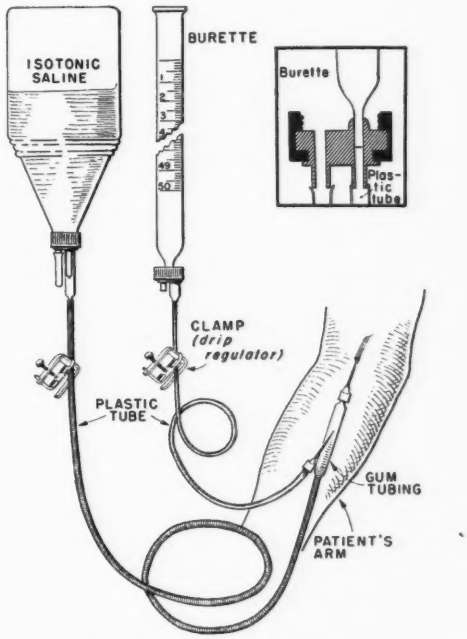

Fig. 1. Schematic presentation of the infusion setup used for serial estimations of blood volume. The insert shows a cross section through the dispensing cap of a secondary venopak to indicate the correct placement of the burette.

The volume of circulating red cells is given by the difference of total blood volume and plasma volume.

Clinical material. Since it was not the purpose of this investigation to study the statistical variations of normal or abnormal blood volumes, but to investigate the applicability of a method, a wide range of values appeared to be desirable. The clinical material used for this study consisted of preoperative patients admitted for minor or major procedures. They were chosen at random, without regard to age, degree of anemia, or preoperative diagnosis.

For the study of serial blood volume determinations during surgical operations, these procedures were first studied in a variety of routine gynecologic operations in which blood transfusions were withheld. The opportunity also presented itself to test the procedure in several radical hysterectomies and pelvic lymph node dissections in which blood re-

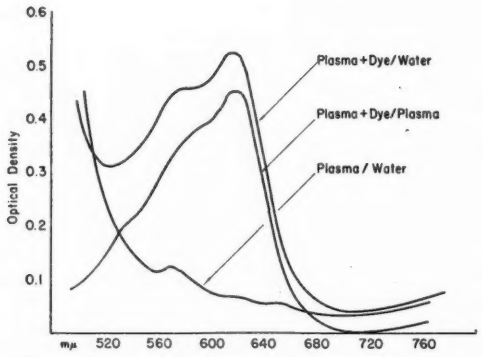

Fig. 2. The absorption curves of Evans blue (T-1824) in plasma compared to the absorption curve of the same plasma sample.

placement and blood volume determinations were carried out simultaneously.

RESULTS

The absorption curves of various lots of the commercial dye T-1824 were determined and were found to be remarkably constant when water or normal saline was used as diluent. Under these conditions the absorption maximum occurs at 605 millimicrons, and the concentration of a given preparation could be determined on the basis of a constant absorption ratio at two different wave lengths.

If plasma is used as diluent the shape of the curve changes with the appearance of a characteristic "shoulder" at about 580 millimicrons, a depression of the maximum for the same dye concentration, and a shift of this maximum to 620 millimicrons (Fig. 2). In an attempt to explain these changes, presumably due to difference in solvent, i.e., the presence of plasma proteins and electrolytes or their effect upon the chromophoric groups of the dye, the curves were compared to those of the same plasma used for the preparation of the dye solution. This comparison does, in part, explain the deviation in the neighborhood of 580 millimicrons but cannot account for the shift, the depression, or the failure of an identical course of these curves below 500 and above 700 millimicrons.

A superficial examination of those absorption curves clearly reveals that the value of the optical density at 680 millimicrons is not one-fourth its value at 620 millimicrons, as reported by Shapiro, regardless of which curve is chosen or whether the solvent is water, saline, or plasma. Nonetheless, all related curves run a strikingly parallel course and it is conceivable that a constant ratio of optical densities could be obtained at more favorably chosen wave lengths.

The optical densities of plasma samples obtained during routine blood volume determinations were recorded at 620, 660, and 680 millimicrons. In Table I the results obtained on 10 such determinations are reproduced and it can be seen that the optical density ratio at 620/660 and 620/680 is not sufficiently constant to justify the use of such a factor for routine purposes.

In order to repeat the determination of the blood volume as many times as possible it would be necessary to determine the lower and upper limits for the amount of dye that can be used for each determination. In the routine procedure, 3.0 to 4.0 cubic centimeters of a 0.5 per cent solution, i.e., 15 to 20 milligrams of dye, have been used and it is known that two successive blood volume determinations can be performed using this or larger amounts of dye. Experiments were, therefore, performed in which the amount of dye used per determination was progressively decreased until checks could no longer be obtained. A series of patients was given 3 or 4 successive infusions of 0.05 per cent Evans blue (T-1824). Satisfactory triplicate determinations were obtained as long as the amount of dye infused per determination remained above 3 milligrams which corresponds to about 1.0 cubic centimeter of 0.3 per cent or roughly 10 cubic centimeters of the test solution. Table II illustrates some of the results obtained by using amounts of dye that ranged from 1.0 to 2.0 cubic centimeters of 0.3 per cent T-1824. No effort was made to reproduce the data obtained by using less than 1.0 cubic centimeter of 0.3 per cent T-1824, for the results were invariably erratic.

As to the upper limits within which the method could be relied upon, no specific data could be obtained. These limits would be determined by the increment in optical density following each successive injection, and the

sensitivity would decrease as the optical density of the preceding control plasma increased. If 4 successive determinations are to be performed, the quantity of dye injected should increase progressively if the same degree of precision is desired. For practical purposes it would seem that, in order to avoid excessive discoloration, 3 or 4 successive determinations should be more than satisfactory to provide reliable data for clinical or research purposes.

However, by using amounts of dye within the limits mentioned, 4 successive determinations do not, by any means, exhaust the potentiality of the method. During operative procedures serial blood volume determinations were performed, an example of which is given in Figure 3. In order to clarify the temporal relations an anesthesia record is reproduced in which the results of blood volume determinations are correlated with blood pressure readings and other significant events. During the procedure the patient received only negligible amounts of 5 per cent dextrose in water but no blood, in spite of the fact that there was ample indication for it. The illustration shows that 8 successive blood volume determinations were made, each utilizing the preceding plasma sample as a control for subsequent determinations.

In contrast to this case, in which no blood was given, Table III represents a balance sheet on blood loss and replacement during a radical excision of a cervical stump with bilateral lymph node dissection. Here, for technical reasons, an excessive blood loss was anticipated. The patient received large amounts of blood during the procedure as dictated by the results of blood volume determinations which were known to the anesthesiologist at 20 minute intervals. The success of this planned administration is clearly demonstrated by the fact that the patient's blood volume, plasma volume, and red cell mass remained reasonably constant during the procedure and, at the conclusion of the operation, was almost identical with the preoperative values.

DISCUSSION

The commercial preparations of Evans blue (T-1824) are available as 0.3 or 0.5 per cent solutions. Since it is difficult or impossible to prepare these solutions on a large scale with sufficient accuracy and stability, the variations in concentration from batch to batch occasionally exceed the error of the method. It has, therefore, been customary to set aside one large batch for routine determinations and to prepare a standardization curve for each new batch. In the calculation of the final result only the ratio of concentrations of injected dye and that in plasma is of significance and reference to the exact number of milligrams of dye injected is unnecessary. The method previously described avoids the use of absolute standards but makes it necessary to determine the amount of dye injected for each series of plasma volume determinations.

TABLE I.—COMPARISON OF OPTICAL DENSITY AT 3 DIFFERENT WAVE LENGTHS ON SERIES OF SAMPLES OBTAINED DURING ROUTINE BLOOD VOLUME DETERMINATIONS

Determination No.	Optical density at				
	620 m	660 mμ	680 mμ	620/660	620/680
1	0.454	.084	.008	5.40	56.75
2	0.552	.110	.018	5.01	30.66
3	0.530	.090	.000	5.88	∞
4	0.543	.070	.000	7.75	∞
5	0.433	.089	.015	4.86	28.86
6	0.420	.115	.032	3.65	13.12
7	0.530	.103	.014	5.14	37.86
8	0.940	.215	.063	4.37	14.92
9	0.489	.106	.024	4.61	20.37
10	0.427	.094	.013	4.54	32.84

Although this makes the procedure somewhat more complex, its reliability is considerably increased. Thus, in effect, a new standard is used for each series of determinations, but the accuracy of its administration is thereby increased. At least in theory, variations resulting from the use of this modification are attributable to physiologic changes or inherent defects of the dye method itself.

Before considering the theoretic aspects of the clinical experiments described, it would seem appropriate to review the major controversial points of the blood volume determination by the dye-dilution method.

The first of these concerns the fact that the validity of the dye dilution method has been

TABLE II.—SUCCESSIVE ROUTINE BLOOD VOLUME DETERMINATIONS USING T-1824 BY INFUSION TECHNIQUE IN CONCENTRATIONS OF ABOUT 0.5 PER CENT

Determination No.	Calculated c.c. of stock solution administered	C.c. of stock solution per c.c. of plasma	Plasma volume
1	1.164	0.000350	3326
2	1.203	0.000388	3101
3	1.347	0.000345	3098
Average			3175
1	1.174	0.000370	3173
2	1.356	0.000415	3267
3	1.160	0.000325	3570
4	1.174	0.000355	3306
Average			3328
1	1.676	0.000600	2794
2	1.740	0.000620	2806
3	1.967	0.000690	2850
Average			2816
1	1.5804	0.000750	2107
2	1.9935	0.000918	2171
3	1.7960	0.000795	2259
Average			2179

The estimation of the concentration of dye in plasma was carried out by reading the first determination against a control, then using the first plasma as control for the second, and so forth.

questioned. It is beyond the scope of this report to review the evidence in its favor, and it should suffice to state that in recent years an overwhelming body of evidence has been accumulated to indicate that the simultaneous use of Evans blue (T-1824) and some of the more complex reagents, e.g., iodinated human serum albumin or polysaccharide S III, give estimates of plasma volume which are, for all intents and purposes, identical.

The second of these controversial points is a phenomenon known as the "cat effect," which has been the subject of numerous investigations reported in the physiologic literature. Thus far, the issue has not encroached upon clinical problems and has, therefore, not been subjected to a critical examination. It is, however, of considerable importance in the problems here encountered.

The subject was first brought to the attention of workers in this field by Cruickshank and Whitfield, who presented evidence that a significant portion of the initially injected Evans blue (T-1824) is phagocytized by the reticuloendothelial system. A portion of the solute (dye) is thus immobilized and would lead to erroneously high values if the dilution of the dye were taken as a measure of the volume. Any additional dye administered after the "saturation dose" would then be used for dilution only and should, therefore, represent a more accurate measure of the plasma volume. The term "cat effect" stems from the fact that Cruickshank and Whitfield's experimental animals were cats, and that attempts to duplicate these experiments on other experimental animals have met with failure. Although the possible influence of the reticuloendothelial system on dye dilution methods has been considered previously by Smith, his observations were limited to the applicability of brilliant vital red. Since the chemical structure of various dyes is a factor of considerable importance in their physiologic behavior, the experiments of Smith are not directly comparable to those of Cruickshank and Whitfield.

If the "cat effect" were correct and consistent, a single determination of plasma volume by the dye dilution method would be subject to an appreciable error. It would mean that any determination performed on a subject whose reticuloendothelial system is not saturated with the dye is useless. Reducing the amount of dye used for each determination might mask the error still further and lead to completely unreliable results.

The analogue of the "cat effect" has never been substantiated in experiments on dogs as shown by Miller, Allen and Semple, Surtshin and Rolf, and Bonnycastle. Because of its potential clinical significance, it has also been investigated in the human. Although Mather reported that the "cat effect" occasionally can be observed in the human, Noble and Gregersen, Campbell, Sokalchuk, and Penman and Reeve and Armin could not concur with this opinion.

None of the authors listed used more than 2 successive injections of dye in order to demonstrate the presence or absence of the "cat effect." In view of the large amount of dye used for each of these determinations, the validity of these experiments cannot be questioned, but it cannot be used as evidence that appreciably smaller quantities of the dye used in our experiments will lead to identical results. It was, therefore, necessary to demon-

strate the reliability and reproducibility of the present modification by a progressive diminution of the amount of dye for each set of 3 or 4 successive analyses.

The data presented indicate that multiple successive plasma volume determinations are reproducible if the limits are maintained within 3 and 6 milligrams of dye per determination. This limitation of the amount of dye is to be sought in the particular method herein described and is not characteristic of the test substance. Allen and Semple have demonstrated that identical values for blood plasma volumes can be obtained on paired estimates in which the second injection was about 10 times greater than the first.

Below the stated limit of 3 milligrams the determination of the optical density becomes too inaccurate even for the most sensitive instrument. When more than 6 milligrams of dye are used the analytic precision is once again reduced, because of the high range of optical density values and because the absolute difference in the disappearance rate of the dye assumes significant proportions.

Although it could be argued that higher concentrations could be employed particularly in view of the experiments of Allen and Semple, the necessary dilutions preliminary to the administration of the dye and the application of correction factors would render the method impractical. It is not possible on the basis of our accumulated data to state an absolute upper limit but to define the practical limitation of this modification.

The data in Table II also show that within the limits stated the "cat effect" is not demonstrable in the human. If it were present and a saturating dose of the dye were necessary before plasma volume determinations, the values for plasma volume should be consistently highest for the first determination and then remain constant or decrease progressively during the second, third, and fourth determinations. Although only a few of the data obtained during these investigations are reproduced in that table, no evidence in favor of the "cat effect" was observed during innumerable routine applications of this method.

An interesting modification of the blood volume determination has been suggested by

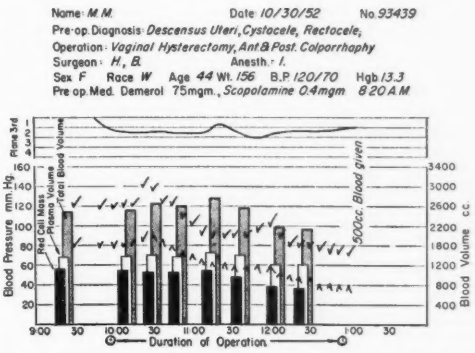
Name: M M. Date: 10/30/52 No. 93439
Pre-op. Diagnosis: Descensus Uteri, Cystocele, Rectocele;
Operation: Vaginal Hysterectomy, Ant. & Post. Colporrhaphy
Surgeon: H, E. Anesth.: I.
Sex F Race W Age 44 Wt. 156 B.P. 120/70 Hgb. 13.3
Pre op. Med. Demerol 75mgm., Scopolamine 0.4mgm 8:20 A.M.
Plane 3rd
Red Cell Mass
Plasma Volume
Total Blood Volume
500cc. Blood given
Blood Pressure mm. Hg.
Blood Volume cc
9:00 30 10:00 30 11:00 30 12:00 30 1:00 30
Duration of Operation

Fig. 3. Reproduction of an anesthesia record obtained during a major gynecologic operation. The results of the blood volume determinations obtained during the operation are superimposed upon the blood pressure readings.

Shapiro, which takes advantage of the alleged constancy of the absorption curve of plasma-dye solutions. If the shape of the absorption curve remains constant then the ratios of the optical densities at arbitrarily chosen wave lengths should remain constant. This could provide a means of determining the concentration of the dye on a chosen sample without a comparison to a control and, therefore, eliminate one venipuncture for each blood volume determination. Specifically it has been stated by Shapiro (based upon unpublished observations by Mallory) that the optical density of Evans blue (T-1824) solutions in plasma at 680 millimicrons is exactly one-fourth the optical density at 620 millimicrons.

Although the absorption curve of Evans blue (T-1824) had been determined by Gregersen and Gibson, Gibson and Evans, and McCord and Ezell, the published data do not lend themselves to a critical examination of the principle here involved. The graphs presented in the report by McCord and Ezell and those by Gibson and Evans were prepared with an entirely different point of view, and neither includes the necessary range of the spectrum. The curves presented by Gregersen and Gibson do include this range but the alleged ratio of 4:1 for the optical densities at 620:680 could not be substantiated with certainty.

Our data represented by the curves of Figure 2 confirm the data of Gregersen and Gib-

TABLE III.—PROTOCOL OF REPEATED BLOOD VOLUME DETERMINATIONS DURING RADICAL EXCISION OF CERVICAL STUMP AND LYMPH NODE DISSECTION

Time	Amount of blood administered (cumulative)	Stock solution used per blood volume determination	Plasma volume c.c.	Total blood volume c.c.
8:35	none	1.682	3004	4800
9:55	650	1.783	2808	4600
11:30	1500	1.918	2959	5140
1:00	2700	1.733	2878	4900
2:30	3500	1.817	2513	4470

Replacement 3500
Net loss 330
Calculated total loss 3830

During this operation an attempt was made to balance blood loss with replacement as indicated by the results of blood volume determinations.

son in all details. Since the ratio of optical densities at selected wave lengths seemed to vary considerably with samples of plasma from different subjects (Table I), in spite of the fact that for each determination the appropriate control was used, it must be concluded that the ratio of optical densities is not a satisfactory measure of the concentration of the dye in plasma.

Several interesting, though fully expected, events were recorded during the application of serial blood volume determinations. With reference to the anesthesia record on patient M.M. it is to be noted that this represents a sequence of events which eventually led to a state of mild, acute hemorrhagic shock. It was followed throughout its developmental phase by a series of blood volume determinations. During the initial stages of the operation the relative and absolute values of the red cell mass and plasma were essentially identical with the preoperative control. Then a slight but significant rise in blood pressure was noted and this was associated with an increase in plasma volume and a slight drop in the red cell mass. The subsequent drop in blood pressure coincided with a moderately severe episode of bleeding which was eventually controlled. This was followed by a slow but persistent fall of the blood pressure in the neighborhood of 95/50 in spite of a sharp but temporary increase in plasma volume and, presumably a compensatory mobilization of red cells. Since blood replacement was avoided during this procedure, the blood pressure showed a persistent downhill course thereafter which mirrored the decline in the red cell and the plasma volume.

Based upon the analytic figures graphically recorded, at the end of the operation this patient had lost roughly 350 cubic centimeters of red cells and the plasma volume had decreased by about 200 cubic centimeters. Twenty minutes after the last blood volume determination the patient was given a transfusion of 500 cubic centimeters of whole blood. The blood pressure then returned to preoperative levels.

The sequence of events described was observed in almost identical fashion on a series of patients and its significance will be discussed elsewhere.

The second clinical example of the application of the method deals with controlled blood replacement during radical procedures. A particularly difficult operation was chosen for this purpose which, for technical reasons, was associated with an excessive loss of blood. Since it was thought that a presentation in the form applied to the preceding case would be of little value, the significant data are reproduced as balance sheet (Table III). Here the patient started with a satisfactory blood volume of 4,800 cubic centimeters, which was maintained within 300 cubic centimeters throughout the operation without significant changes in blood pressure. During the procedure the patient had received 3,500 cubic centimeters of whole blood and at the conclusion of the operation a deficit of 300 cubic centimeters was recorded, which was attributed to a net loss of plasma since the red cell mass was at about preoperative levels.

SUMMARY AND CONCLUSIONS

1. A modification of the dye dilution method for the determination of plasma volume is described. It consists of an increased accuracy in the administration of the dye thus permitting a reduction of the amount of dye to be used for each determination (3 to 4 mgm. instead of 15 to 20 mgm.).

2. Because of this reduction of the amount of dye, duplicate, triplicate, or quadruplicate

estimations of plasma volume can be carried out each using the preceding plasma samples as a control. Additional evidence is presented that the "cat effect" does not exist in the human.

3. A simplification of the blood volume determination based upon the alleged constancy of plasma-dye solutions was investigated. It was concluded that the ratios of optical densities is not a reliable measure of the dye in plasma.

4. Examples of the application of serial blood volume determinations during major operative procedures are presented.

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PEPTIC STENOSIS OF THE ESOPHAGUS

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BENIGN stenosis of the esophagus may be due to a multitude of causes such as that due to drinking lye, but, in a large proportion of cases, there is no clear-cut cause and the present study concerns 100 patients in this group.

The patients were chosen consecutively from the records after the exclusion of those suffering from lesions which were due to lye, acid, trauma by foreign bodies, scleroderma, pemphigus, pellagra, Plummer-Vinson syndrome, achalasia of the cardia, and those which followed operation for carcinoma of the stomach or esophageal varices. The result is that these cases represent stenosis of unknown origin. All were seen at some stage of their illness in the endoscopy clinic and all were proved by esophagoscopy to have stenosis. It has been customary to include these under the heading of benign stenosis, but, as a result of the examination of these patients and perusal of the literature, it seems desirable to describe this condition as peptic stenosis of the esophagus.

It was also hoped to gain some clear indications as to the best type of treatment for individual patients and, while certain conditions point inexorably to medical and others to surgical treatment, the result of this study shows that many patients can be treated successfully by either method.

CASE MATERIAL

Of the 100 patients 60 were males and the average age on first attendance at this hospital with the complaint of dysphagia was 56.8 years (range 15 to 85 years). Forty were females and their average age on first attendance at the hospital with the complaint of dysphagia was 60.1 years (range 36 to 80 years). As some had had symptoms for many years, Table I shows the age of the patients at the time of *onset* of dysphagia.

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Symptomatology. As this report concerns only those with proved stenosis, all patients suffered from dysphagia. One woman with aphasia was recognized through failure to pass a stomach tube. One patient was admitted a few hours after his first attack of dysphagia and, at the other extreme, 1 man was seen only after 40 years of difficulty in swallowing. The average duration of symptoms when first seen was 4 years and 4 months. Table II shows the distribution and it will be seen that 47 per cent of patients had had dysphagia for less than 9 months.

The severity of dysphagia on first admission was assessed as follows: mild—some "sticking" of food—11 cases; moderate—only able to take fluids and soft foods all the time (or, in some cases, more severe disability but less constant)—54 cases; severe—only able to take fluids (or unable to swallow anything)—35 cases.

In 51 cases the degree of dysphagia varied, in some markedly. In 60 cases dysphagia became progressively more severe generally from the time of its inception until the patient's admission. In 9 cases dysphagia which had been relatively constant or else had only been present intermittently, became steadily more severe for some months prior to admission.

Vomiting and regurgitation occurred in 42, epigastric pain in 30, and odynophagia in 17 at the time of admission. Twenty-two patients had a history of what appeared to be a significant degree of heartburn (9 of these had roentgenologic evidence of esophageal ulcers, 10 had no evidence of ulceration, and 3 were doubtful).

Anamnesis. Twenty-two patients had had a surgical operation requiring anesthesia and hospitalization within 5 months of the development of dysphagia. Fifteen of these began to have difficulty in swallowing while they

were convalescent from the operation. In 5 cases an inlying gastric tube was used (data on this point for the other patients are not available as many of the operations were done at other hospitals) (Table III).

Fourteen patients suffered from gallbladder disease at some stage of their lives, the type of operation or disease being recorded as follows: cholecystectomy (8), gallbladder colic (2), cholecystitis (2), "gallbladder drained" (1), gallstones (1).

RESULTS OF EXAMINATIONS

Esophageal hiatus hernias. Eighty-five patients had a hiatus hernia and there were 2 probable cases. These were generally shown on several occasions by roentgenologic examination and some were confirmed by esophagoscopy or operation. Sixty-nine had a sliding type of hernia. The reports for the others do not state the exact kind present but in none was a paraesophageal hernia noted. The size of the hernias varied, the average for the 20 cases in which size was recorded being 5 centimeters in length.

Esophageal ulcers. On roentgenologic examination, 40 patients were considered to have esophageal ulcers and a further 12 had doubtful evidence. Fifteen of these patients were operated on and the ulceration confirmed. Two who had not shown roentgenologic evidence of ulceration were found to have ulcers at operation.

Gastroduodenal ulcers. Forty patients showed roentgenologic evidence suggestive of present or past duodenal ulceration (this was confirmed at operation in 4 cases and there were 3 suspicious cases). Four others had symptoms but no x-ray confirmation. One patient was examined at another hospital and was reported to have a peptic ulcer but the site was not stated.

Biopsies taken through the esophagoscope. One hundred and nineteen biopsies were taken from 80 patients. Forty-nine of these showed gastric mucosa in one or more biopsies (62 per cent of patients biopsied), the rest of the specimens showed acute or chronic inflammation of esophageal mucosa.

Operation specimens. Thickened periesophageal inflammatory tissue was present in the 20 cases in which resection was done and in the 3 cases in which cardioplasty or repair of a hiatus hernia was performed in this hospital. Dr. R. H. Sweet, who did most of the operations, considered this to be a characteristic finding. Twenty patients had a resection of the lower esophagus and cardia with subsequent esophagogastric anastomosis. Table IV summarizes some of the pathologist's findings.

In all cases the site of the stenosis was in the region of the cardia or just above it.

In the 5 cases in which a measurement was made, the length of the stenosis averaged 2.1 centimeters. In most of the others the total length of resected esophagus was noted but not the actual length of narrowing which was probably considerably less, such cases are indicated by the sign "<" in the table.

In the 2 cardioplasty cases, the surgeon estimated the stricture to be a "few millimeters" in one and about 1.5 centimeters in the other.

Of the 16 cases in which a measurement of the thickness of esophageal wall was made the

TABLE I.—AGE AT ONSET OF DYSPHAGIA

Age, years	No. of males	No. of females	Total No.
0–10	1	—	1
11–20	2	—	2
21–30	3	—	3
31–40	2	6	8
41–50	11	8	19
51–60	13	13	26
61–70	23	11	34
71–80	4	2	6
81–90	1	—	1
Totals	60	40	100

TABLE II.—DURATION OF DYSPHAGIA

Duration of dysphagia	No. of patients
0—7 days	3
1—4 weeks	8
1—3 months	11
3—6 months	12
6—9 months	4
9—12 months	9
1—2 years	16
2—3 years	2
3—4 years	8
4—5 years	4
Over 5 years	23

TABLE III.—SURGICAL OPERATIONS PRIOR TO ONSET OF DYSPHAGIA (22 PATIENTS)

Patient's No.	Type of operation	Lesion	Time after operation when dysphagia began	In-lying gastric	
				Used	Days
2	Resection of rectum	Carcinoma	5 months		
3	Partial gastrectomy	Duodenal ulcer	1 month	+	14
4	Gastrostomy	Carcinoma	Convalescence		
16	PGE and vagotomy	Duodenal ulcer	1 month	+	
19	Lysis of adhesions	—	Convalescence		
24	Cholecystectomy	Cholecystitis	Convalescence		
25	Resection of rectum	Carcinoma	2 months		
32	Partial gastrectomy	Duodenal ulcer	Convalescence	+	2
38	Partial gastrectomy	Duodenal ulcer	Convalescence		
42	Drainage	Diverticulitis and peritonitis	Convalescence	+	120
51	? Resection of cecum	Carcinoma	1 month		
73	Cholecystectomy	Cholecystitis	Convalescence	+	?
79	Herniorrhaphy	R. ing. hernia	Convalescence		
80	R.U. lobectomy (lung)	? Lymphoma	Convalescence		
82	Repair and drainage	Perf. duod. ulcer	1 month		
84	Cholecystectomy	Cholecystitis	Convalescence		
88	Feeding gastrostomy	Duodenal ulcer	Convalescence		
91	Cholecystectomy	Cholecystitis	Convalescence		
92	Cholecystectomy	Cholecystitis	2 months		
93	L.L. lobectomy (lung)	Bronchiectasis	Convalescence		
94	Appendectomy	Appendicitis and peritonitis	Convalescence		
98	? Excision	? Duodenal diverticula	Convalescence		

mean was 8.0 millimeters with a range of 5 to 10 millimeters.

The mean circumference of the esophagus of the 9 cases in which a measurement was made was 2.7 centimeters.

Ulceration of the esophagus was present in 17 of the specimens (3 had multiple ulcers) and varied from shallow to deep penetrating ulcers.

Other histologic findings included chronic and often acute inflammation present in all cases. Fibrosis was noted in 10 specimens. The muscular layer was increased in 7. Gastritis (in 1 case limited to a small area of the adjacent cardia) was present in 2 and noted to be absent in 6 specimens.

RESULTS OF TREATMENT

Medical (patients followed for at least 1 year after last treatment). Treatment by bouginage alone will be considered here, although all patients were also put on a special diet and generally on antispasmodics and antacids. Thirty-four patients have been followed and were still alive at least 1 year after the last treatment by bouginage. One patient had been followed for 14 years and the mean was 4 years 2 months.

The results were as follows: good—17 patients (all able to swallow food normally or with only occasional slight difficulty); fair—15 patients (able to swallow liquids and soft foods normally but generally having difficulty with more solid food); unchanged—2 patients.

The mean duration of dysphagia before bouginage was started was 4 years 3 months and 3 weeks with a range of 3 weeks to 20 years. The degree of dysphagia on first admission was mild in 10, moderate in 18, and severe in 10. The degree of stenosis by the estimated diameter of the lumen at esophagoscopy was as follows: 6 millimeters or over in

TABLE IV.—OPERATION SPECIMENS

Patient No.	Site of stenosis	Length of stenosis, cm.	Thickness of wall, mm.	Ulceration of mucosa		Pathologist's description
				Present	Type	
9	Just above gastric mucosa	<3.5	7	−	—	Stricture of esoph. chronic inflammation
10	Max. narrowing 2 cm. above esophagogastric junction	3.0	9	+	?	Acute esophagitis with ulceration
13	Cardia	<5.0	8	+	Acute peptic	Peptic ulcer of esoph. with fibrosis
14	Cardia and above	<10.0 (includes stomach)	?	+	Shallow peptic	Peptic ulcer of esoph. chronic inflammation and fibrosis
19	Just above cardia	<4.5	6	+	Shallow	Acute and chronic inflamm. with ulceration and fibrosis
20	Cardia	2.3	5	+	Multiple superficial peptic	Peptic ulcers of esoph. chronic esophagitis with stenosis
31	Just above cardia	<3.5	10	+	Peptic, just above gastric mucosa	Peptic ulcer of esoph.
46	Cardia and lower esophagus	"short"	8	+	2 shallow (0.3 cm. diam.)	Benign ulcer of esoph.
49	Just above cardia	3.8	?10	−	—	Chronic inflammation and fibrosis
66	Esophagogastric junction	<2.2	10	+	Deep 2.5 × 2.0 mm.	Healing ulcer of esoph. with stricture. Chronic esophagitis and gastritis
68	Esophagogastric junction	<2.2	11	+	No fibrinoid layer	Acute and chronic ulceration of esoph. with ulceration and stricture and ulceration
69	At and above cardia	<3.0	8	+	Shallow 1.5 cm. diam.	Chronic inflammation with ulceration
71	1 cm. above cardia	<4.5	8	+	?	Stricture of esoph. acute and chronic inflamm. with ulceration
73	Just above cardia	<5.5	10	+	?	Stricture: acute and chronic inflamm. with ulceration
79	2.2 cm. above cardia	2.5	?	+	Penetrating peptic	Acute peptic ulcer of esoph. chronic inflamm. and fibrosis
80	Region of cardia	<3.5	8	+	Perforated	Chronic inflammation with ulceration and fibrosis (stricture)
81	Region of cardia	<3.5	5	+	Peptic shallow	Chronic esoph. with peptic ulcers
82	"Lower end of esoph."	<6.0	?	−	—	Acute and chronic inflamm. with fibrosis
87	Cardia	<5.0	5	+	?	Chronic esoph. with ulceration
94	Esophagogastric junction	<3.5	?	+	Shallow only penetrates mucosa	Severe chronic esoph. with ulceration

8 cases; 4 to 6 millimeters in 7 cases; 0 to 3 millimeters in 13 cases. (In 5 cases an estimate was not made.)

The mean number of bouginage treatments was 7 and the range was 1 to 54. The mean length of treatment, i.e., the time from the first to the last, was 11½ months and the range was from 0 (i.e. 1 treatment) to 13 years and 10 months. Twenty-six patients were given less than 1 year's treatment by bouginage.

Surgical (patients alive and followed for at least 1 year since operation). Twelve patients in this group were treated by resection of the lower esophagus and cardia followed by esophagogastric anastomosis and 2 by cardioplasty. The average follow-up period was 4 years and 3 months with a range from 1 year and 6 months to 7 years and 7 months.

The results were as follows: good—11 patients (includes 1 cardioplasty); fair—2 patients (includes 1 cardioplasty); unchanged—1

TABLE V.—RESULTS IN PATIENTS SEEN AT LEAST 1 YEAR SINCE LAST TREATMENT

	Good No. cases	Fair No. cases	Unchanged No. cases	Total No.
Bouginage	17	15	2	34
Resection	10	1	1	12
Cardioplasty	1	1	—	2
Totals	28	17	3	48

patient (subsequent good response to bouginage).

The degree of dysphagia before operation was mild in 1, moderate in 8, and severe in 5. (The patient with only mild dysphagia was operated on for hiatus hernia and found to have marked inflammation and a mass above the cardia so resection was carried out.)

The degree of stenosis by the estimated diameter of the lumen at esophagoscopy was as follows: 4 to 6 millimeters in 1 case; 0 to 3 millimeters in 8 cases. (In 5 cases an estimate was not made.)

The mean number of bouginage treatments before operation was 7 and the range was 1 to 31.

Table V shows the results of medical and surgical treatment of all the patients who have been followed and were alive at the end of 1 year after the last treatment.

Unsatisfactory results of treatment. Fourteen patients showed an unsatisfactory response to treatment. (a) Medical.—One patient died from spontaneous perforation of the esophagus and another from rupture at esophagoscopy. One patient wrote saying that his condition was worse but, due to home difficulties, he could not attend for further treatment at present. Five patients were unchanged after medical treatment, 3 having died of causes unrelated to the esophageal lesion and 1 from an unknown cause. One patient was alive 3 years, 8 months after the last treatment but said that symptoms were unchanged. (b) Surgical.—Three patients died shortly postoperatively. Two had a recurrence of dysphagia postoperatively. (One had a second resection operation and is doing well and the other is responding to bouginage treatment.) Two patients had no change in their symptoms following recurrence of a hiatus hernia after operation. (One was operated on in 1915 and eventually died from carcinoma of the larynx, the other has only mild symptoms.)

Present status of all patients. Of the 100 patients in this series, 46 per cent had a good or fair result from treatment of the stenosis, 33 being alive at least 1 year after the last treatment (medical or surgical) and 13 having died from intercurrent disease but having required no treatment for at least a year before their deaths. (This includes 1 patient, listed as an unsatisfactory result of surgery in Table V, who subsequently responded well to bouginage.)

Three per cent of the patients were unimproved after a lapse of at least 1 year since the last treatment.

Twenty-seven per cent of the patients have not completed 1 year since the last treatment and, of these, 12 died from intercurrent disease (6 died from pneumonia which may, conceivably, have been due in some cases to aspiration related to the stenosis).

For 9 per cent there is insufficient data to assess their status although 4 of them are known to be dead.

The remaining 5 per cent died as a direct or indirect result of the stenosis (3 postoperative, 1 spontaneous perforation, and 1 rupture at esophagoscopy).

ETIOLOGY

Incidence, age, and sex. Table I shows that in 78 per cent of the present series, the age of onset was between 40 and 70 years of age, i.e. at a later time than symptoms of peptic ulcer of the stomach and duodenum arise. The reason for this is believed to be that most patients with the ulcer diathesis do not generally have sufficient esophageal reflux to cause peptic stenosis until a hiatus hernia develops. The sex incidence shows a higher ratio of females to males than is usual in cases of peptic ulcer of the stomach and duodenum.

The significance of gastric juice. In the present series there had been vomiting, often of marked degree, in 29 cases before dysphagia began. The causes were as follows: peptic ulcer of duodenum or stomach in 5 cases; pyloric stenosis in 5 cases; unknown causes in 5 cases; postoperative in 3 cases; pregnancy in 1 case.

In addition to these cases, it is probable that vomiting or regurgitation occurred in 6 alcoholic patients and in 1 patient who was comatose and severely ill with jaundice and myocardial infarction in another hospital. As already noted, 14 patients had had gallbladder disease and, although vomiting was not marked in any of these, it may have occurred at times. We believe that the presence of acid gastric juice in the esophagus is an essential feature for the development of this type of stenosis, hence the term "peptic stenosis." The means which allowed gastric juice to remain for an abnormal time in the esophagus of the other cases will be considered below.

The significance of ectopic gastric mucosa in the esophagus. This is a more controversial and less well documented subject than the question of the harmful effects of gastric juice. While isolated islets of gastric mucosa surrounded by esophageal tissue are undoubtedly ectopic, it appears that the line of junction between the esophageal and the gastric is often irregular so that tongues of gastric mucosa may project upward and tongues of esophageal mucosa may project downward. An associated difficulty is that the cardia is a somewhat ephemeral concept better recognized physiologically than anatomically.

As noted previously, 49 of the 80 patients in the present series who had a biopsy taken showed gastric mucosa in 1 or more specimens. Certainly in some of these cases, and probably in all, the biopsy was taken from near the cardia. The invariable inflammation and the anatomic deformity means that estimation of the exact site of the biopsy with respect to the cardia is sometimes difficult. However, in most cases of specimens resected at operation it was noticeable that there was no inflammation of the adjacent gastric mucosa and none showed ectopic gastric mucosa of any significant extent in the lower esophagus.

Thus we believe that, while there is good evidence in the literature that ectopic gastric mucosa is sometimes the main factor in producing sufficient gastric juice in the esophagus to cause inflammation and stenosis, we could not incriminate this mechanism in this series. The term peptic stenosis covers cases due to ectopic mucosa and to reflux of gastric juice.

The site of the stenosis relative to the cardia. This is a point of great importance, for, if gastric juice be the main factor, then the lesion is likely to occur just above the cardia. If, as we found, all or probably all lesions occurring in this region and their peptic genesis are not accepted then some other theory will have to be advanced for this peculiar location. It may be suggested that the area is more vulnerable to trauma from ingested food because of the anatomic arrangement and the delay in the passage of the bolus.

Twenty-three of the present series had an operation in this hospital with 20 resections, 2 cardioplasty operations, and 1 repair of hiatus hernia alone. In all cases the site of the stenosis was in the region of the cardia, generally just above the junction of the esophageal and gastric mucous membrane (see Table IV). Of the 77 patients who did not have an operation, an attempt was made by correlation of the roentgenographic and esophagoscopic findings to determine the relationship of the stenosis to the cardia and in 65 of these the lesion was within 2 to 3 centimeters proximal to the cardia. In 9 cases the exact site could not be determined, and in 3 the lesion and the cardia appeared to be separated by over 5 centimeters. The invariable findings at operation are significant and mistaken roentgenologic interpretation may account for the doubtful cases. In 2 cases the roentgenologist's report was that of a high stricture with normal esophagus below but, at operation, the structure distal to the lesion was shown to be a tubular portion of herniated stomach.

We believe that in all cases of peptic stenosis of the esophagus the lesion is just above the cardia and that if a stenotic lesion can be proved to be well above the cardia the diagnosis should not be accepted unless there is extensive ectopic mucosa in the involved area.

The significance of acquired esophageal hiatus hernia. The figures for esophageal hiatus hernia in the present series have been given (85 certain and 2 probable) and most likely all were of the sliding type. The majority of patients fell in the age group when the development of hernias is most common. Regurgitation into the esophagus was not specially looked for at roentgenologic examination

and the patient's symptoms are not a reliable guide unless gastric contents reach the mouth.

While it is not suggested that a hiatus hernia is sufficient to account for significant regurgitation in all cases, when it does occur it is a likely factor. The 13 cases with no hernia on roentgenologic examination were then analyzed to see what other factors might be operative. In 6 cases dysphagia began immediately or shortly after an operation, in 1 during a severe illness with a long period of coma, 1 patient had frequent drunken episodes, 1 had frequent belching associated with a duodenal ulcer, and 1 had pulmonary tuberculosis. In another case the esophagus was considered to be normal below the lesion but, as explained before, it is quite likely that the patient really has a hiatus hernia. In other words, the great majority of the patients in the present series had an obvious or adequate reason for regurgitation whether associated with a hiatus hernia or not. The hiatus hernia is thus an important cause of significant gastric reflux and it accounts for the age incidence of the development of peptic stenosis.

The coexistence of gastroduodenal ulcers and stenosis of the esophagus. This relationship may be interpreted in two ways: either the "ulcer diathesis" is prerequisite for the development of esophageal stenosis or else it is merely an aggravating factor. The incidence of duodenal ulcers is certainly much higher in this group than in the general population but over half the patients had no roentgenologic evidence of ulceration nor histories suggestive of such trouble. Another argument against an inevitable association with the ulcer diathesis is that 6 patients without evidence of duodenal ulcers developed esophageal stenosis postoperatively.

Thus it seems that the ulcer diathesis greatly predisposes to the development of esophageal stenosis by virtue of the increased secretion of gastric juice and greater liability to gastric reflux even in the absence of pyloric stenosis. It may also be that the ulcer patient has changes in the mucosa of the lower esophagus which make it less resistant to acid-peptic action. But while this question cannot be settled on the available evidence, it seems that peptic stenosis of the esophagus can occur in the absence of the ulcer diathesis.

The significance of esophagitis and esophageal ulceration. All the patients in the present series showed inflammation of the lower esophagus on direct examination and all biopsy specimens showed evidence of acute or chronic inflammation. Except in 1 case these did not give evidence of peptic origin. Forty patients had roentgenologic evidence of ulceration, 15 being proved at operation and 2, which had not been shown by barium examination, were found at operation. The 20 operation specimens showed acute or chronic inflammation in all cases and ulceration in 17 cases, these varying from mucosal erosions to penetrating ulcers. In 6 cases the pathologist reported the ulcers to be "peptic."

Other factors—surgical operations, gastric suction tubes, and alcoholism.

Table III shows that 22 patients in this present series had a major operation within 5 months prior to the development of dysphagia and, of these, 15 began to have difficulty during convalescence. This incidence is so high that it appears to be significant especially when one notes that 6 of these patients had no hiatus hernia. It seems reasonable to suppose that the operation and the recumbent posture following it allowed relaxation of the cardiac sphincter with regurgitation of gastric juice. In only a few cases has one a history of excessive vomiting which, in itself, would be sufficient to account for the lesion. The absence of a hiatus hernia in certain patients is most important as showing that this factor could not be held to account for regurgitation.

TREATMENT

Evaluation of any form of treatment must take into account the erratic course of the disease before irreversible fibrosis occurs—a course as irregular as that of duodenal ulcer. Spasm superimposed on organic changes and often precipitated by emotional stimuli account for the acute exacerbations, and, presumably, edema may have a similar effect.

Bouginage. Most patients have come for treatment at a stage when mechanical relief is necessary and so the effects of antispasmodics, antacids, and diet, while generally used, are likely to be of secondary importance and their effect is difficult to evaluate.

The results of bouginage of the present series have been described, 34 patients having been followed for an average of 4 years and 2 months since the last dilatation, 17 having a good result, 15 a fair result, and 2 being unchanged. An attempt was made to see if there could be any correlation between the various factors and the results of both medical and surgical treatment. From consideration of the length of history, degree of stenosis, number of bouginage treatments, and time over which treatment was spread, no correlation was found in the series, but this may be because the number of cases is too small to indicate a relationship. Bouginage is naturally the first method of treatment which ought to be used in all cases once the diagnosis is established. Surgical treatment is only indicated if bouginage fails, if there is severe hemorrhage, or if there appears to be risk of penetration of an ulcer. If carcinoma cannot be excluded or if the patient is averse to repeated bouginage then resection is indicated. The value of bouginage is shown by the number of patients who began with severe dysphagia and marked stenosis and yet responded to only a few treatments. In 1 case resection was contemplated because of the severity of the condition but the patient subsequently responded satisfactorily to dilatation. The risks of medical treatment must, however, be considered. In this series, 1 patient died from spontaneous perforation of the esophagus and another from rupture following esophagoscopy. "Blind" bouginage i.e., the use of sounds without a guiding thread must never be done. In some cases it may be preferable to do repeated dilatations under direct vision and under general anesthesia if desirable.

Resection and esophagogastric anastomosis or plastic operations. Of the present series, 20 patients were treated by resection and esophagogastric anastomosis. Three died postoperatively (1 from pulmonary embolism and myocardial infarction, 1 from fistula formation and pyloric obstruction, and another died from pulmonary tuberculosis having been in very poor condition before the operation). Two patients had a recurrence of stenosis, one having a second operation with satisfactory result and the other responding to medical treatment. Two patients required pyloroplasty following resection, one having a fair result 1 year and 8 months after the second operation while the other's progress is not known. Of the remaining 13 patients, 9 were alive with no dysphagia at least a year after the operation, 1 had no dysphagia for 5 months after the operation and then died from intercurrent disease, and 3 had a fair result but had been followed for less than 1 year.

Two patients were treated by cardioplasty, one having a good result for 1½ years after the operation and then dying from intercurrent disease and the other having a fair result with observation over 6 years and 3 months.

The results of resection or cardioplasty for those patients followed for at least 1 year after operation (average follow-up of 4 years and 3 months) have been given in the foregoing and are summarized in Table V. These figures, small though they are, suggest that resection and esophagogastric anastomosis may be a very good operation. Both patients who had a severe recurrence following resection were operated on in 1945 and more recent surgical results have been better probably owing to wider resection extending beyond the area of esophagitis. Some of the patients with good results have shown a fair amount of fluid in the thoracic portion of the stomach on roentgenologic examination but this did not appear to be causing trouble.

Resection and esophagojejunostomy. While it is unlikely that intestinal juice is as harmful to esophageal mucosa as gastric juice, there is some evidence that it can be injurious as shown by the occasional development of stenosis following resection of the stomach and esophagojejunostomy for carcinoma involving the cardia. At least 4 such cases have been seen in the endoscopy clinic within recent years but it is possible, of course, that the stenosis was due to other mechanisms.

Vagotomy. In the present series, 1 patient had vagotomy and a posterior gastroenterostomy done for a duodenal ulcer but, instead of preventing stenosis, this operation was followed by the development of esophageal stenosis.

Gastric resection. Five patients in the present series had had gastric resection performed

for duodenal ulcer *prior* to the development of dysphagia and esophageal stenosis and so in these cases it was obviously of no prophylactic value. One patient had gastrectomy following the development of peptic stenosis but it was without effect on the stenosis. Thus while we believe that the operation is theoretically justified insofar as it reduces the volume of gastric secretion there is inadequate evidence as to its prophylactic or curative value.

Repair of hiatus hernia. In the present series 5 patients had repair of a hiatus hernia without other surgery except that 1 was combined with a cardioplasty. Of these, 3 developed a recurrence of the hernia and 1 had repair of the hernia because of bleeding but the peptic stenosis had previously been treated satisfactorily by bouginage. It is thus not possible to draw conclusions from these cases but it is reasonable to say that hiatus hernia is one of the etiologic factors as 85 per cent of the present patients had such a hernia. If hiatus hernia exists alone and causes symptoms which are not relieved by posture and diet then operation is clearly indicated irrespective of the possible development of stenosis.

CONCLUSIONS

Peptic stenosis of the esophagus is due to abnormally prolonged contact of gastric juice with the region above the cardia. It can occur in a normal individual but is more likely in those with the ulcer diathesis.

Gastric juice occurs in the lower esophagus to an abnormal extent as the result of the following factors: (1) esophageal hiatus hernia of the sliding type; (2) excessive vomiting or regurgitation from relaxation of the cardia.

Esophagitis was present in all of our 100 cases, and 42 showed evidence of ulceration.

In view of these findings, it is desirable to repair hiatus hernias which are causing symptoms and do not respond to other measures.

In theory, gastrectomy for gastroduodenal ulcers ought to be of value in preventing the development of peptic stenosis of the esophagus but the present series does not support this thesis.

Bouginage, following the swallowing of a thread, is satisfactory in most cases. It should be combined with dietetic treatment, antispasmodics, and antacids.

There are three indications for surgery: (1) failure of bouginage, (2) severe hemorrhage, and (3) perforation.

EDITORIAL

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WHAT IS "TEACHING" IN GRADUATE SURGICAL TRAINING

SINCE the end of World War II there has been quite a hurried expansion of available residency programs. This has been brought about as a result of the large number of young men, veterans and others, who wish to take graduate surgical training. The trend is a challenge to those in charge of the teaching programs. Certification by the American Boards is sought by all not only for general recognition but because hospital governing boards, following the example of the Armed Forces, the Veteran's Administration, and other organizations are using certification as the only practical yardstick by which to evaluate competence. Among the group seeking surgical careers are many who are older, some who are married, and who necessarily have to consider economic factors. Out of this situation have developed certain deficiencies in residency training programs which have prompted this discussion as to just what "teaching" means.

The deficiencies seem to fall in three groups. First, hospitals which have not had the residency plan before and have built up a program from scratch, so to speak, very often have exploited the residents for the interests of the busy practicing attending staff. There has been an inadequate grasp of the meaning of such a program. They have not fully realized that the acceptance of a training program demands a sacrifice of far more time than is saved by the presence of these residents. There is often insufficient graded responsibility, since the members of the attending staff do not have time to oversee the slower work of the residents. From the resident's angle it would be far better that his chief make rounds on 8 patients per day with time for discussion than upon 35 who are seen simply for routine orders in the course of a busy practice.

Second, didacticism, unfortunately, sometimes becomes synonymous with "teaching" in the graduate sense. Residents request lectures, movies, and formal presentations leading to a passive adsorption of facts; they should have stimulation of active thinking processes leading to absorption of knowledge. These planned sessions seem to be much more on the undergraduate level than on the graduate and are often the result of an incorrect interpretation of the meaning of "teaching." The graduate student should be able to read the literature intelligently and to obtain his information from contemporary authorities. In scientific conferences he should be a colleague, not a student. Third, the resident has little chance to develop maturity of judgment and thought if he is given no definite responsibility. He should be in full charge of writing

orders, on private as well as ward patients, throughout his training—a policy which insures active thinking and close association with his attending men. And during his final year he should have complete responsibility both administratively and professionally, under supervision, of the available ward service, which implies most of the actual operating. This he can do competently if his preliminary years have been well directed and if a ward service is unselfishly supplied to him.

These deficiencies appear to be the fault primarily of the teachers and the hospitals. This is not altogether true, however, since the resident has fostered certain of them. He often insists on didacticism in order to assimulate facts which will enable him to pass the Boards, quite without regard to the adequacy of his training and general development. Economic considerations have forced him to seek posts offering high stipends where the chance of being exploited is greater. He considers jobs where the eventual reward may be staff appointment, instead of jobs where the training is best. We feel sometimes that this materialistic attitude threatens to change the art of medicine into the business of medicine.

To cope with these deficiencies several general statements are offered. The aims of the residency should be, first, to supply ample experience and graded responsibility in the various fields so that the young man may realize, in 3 to 5 years, maturity of judgment, confidence in his own ability, and technical competence; second, to encourage him to read and learn intelligently from his cases as he sees them, not to depend upon formal lectures for his "teaching"; third, to de-emphasize examination requirements and to emphasize adequate training; fourth, to expose the resident to the methods of medical investigation and to actual participation in research, if possible; and fifth, to broaden his general background.

We may pass over the regular surgical, pathologic, and death conferences which are a part of almost all well-run hospitals and are assumed to be valuable—indeed essential; and we may be assured that in the larger areas there will be many scientific meetings outside the hospital that the residents may attend. In the hospital itself emphasis should be placed upon the patients, their preoperative evaluation, need for surgery, their immediate care and comfort; and above all, upon the recognition and treatment of complications. Too often surgical rounds consist of presentations of interesting material instead of discussions of the fundamental problems of the patients that do not do well, who have had an erroneous diagnosis, whose course has been jeopardized by poor care, or who have died. The obligation of the staff is to see to it that there is time for constant daily informal discussions; that the material is adequate and is properly studied; and that the resident has sufficient increasing responsibility to insure maturity and adequate experience.

In addition, there would seem to be many matters which might well be made a part of the surgical training and could be offered in monthly meetings. These seminars would be directed at the broad problems of medicine today—such subjects as the types of surgical practice, trends in the patterns of medical care, the preparation necessary for various kinds of careers. Leaders in various fields could be asked to direct these discussions. A few illustrative topics may be mentioned: industrial surgery; surgery in a large city; surgery in country areas; academic careers; research careers; group practice; government medicine. Then there are economic subjects which would be worth while for inclusion in such seminars: partnerships; estate planning; financing of medical schools; the cost of medical care and possible solutions. Finally,

to combat what seems to be a growing materialistic viewpoint toward medicine, there might be discussions presided over by a clergyman or other qualified person on the moral and spiritual aspects of the physician's life.

This, then, is a plea to encourage the surgical resident to become a true graduate student and to gear his sights as high as possible; a plea to the hospital staffs conducting residencies to realize the responsibilities and sacrifices involved with the hope that the present high standards of surgery in this country may be maintained and surpassed.

SAMUEL P. HARBISON

THE SURGEON AT WORK

MODERN CONCEPTS OF INTRAPERITONEAL DRAINAGE

ELY ELLIOT LAZARUS, M.D., F.A.C.S, VICTOR BAUM, M.D., F.A.C.S., and LESTER BREIDENBACH, M.D., F.A.C.S., New York, New York

THE frequency with which the question of the use of drainage in the course of intra-abdominal surgery has arisen has prompted this study. We were impressed with the paucity of articles written on this subject within the past 10 years, although prior to that time many had appeared. Information given in current textbooks of surgery and of postoperative care is often vague and confusing, conflicting and inconclusive.

Recent articles and texts on the subject of drains are essentially repetitious. There appears to be unanimity of opinion as to the indications for drainage in intraperitoneal infections and for uncontrollable oozing. The subject of prophylactic drainage as well as the time and method of removal of drains, however, is in controversy. The matter of drainage of uncomplicated biliary tract surgery is a complicated one. Opinions range from always to almost never. Most surgeons believe that prophylactic drainage is indicated because of the possibility of seepage of bile from the gallbladder bed or from aberrant bile ducts.

The subject of removal of the drain too is a controversial one. There is no agreement either on the time or the method of removal. Some authors suggest long, and others suggest short, periods for drainage. Some suggest that complete removal of a drain is better than successive shortenings.

Drains are not without their complications. They are actually foreign bodies and, as such, cause foreign body reaction in the tissues surrounding them, with considerable exudation and drainage. In addition, hernias, fistulas, and obstruction have been mentioned as other complications.

PRESENT CONCEPTS

In an effort to determine the present concepts of intraperitoneal drainage, a questionnaire was sent to 100 leading surgeons, heads of departments of surgery, throughout the country. Sixty-two replies were received (62 per cent). The questionnaire included questions as to whether routine drainage of the gallbladder area following cholecystectomy was used, whether the duodenal stump was routinely drained following subtotal gastrectomy, whether localized intraperitoneal abscesses and generalized peritonitis were drained, and whether drainage was used when retroperitoneal tissues were exposed and in the presence of uncontrollable intraperitoneal oozing. Table I shows, by geographic location, the number and percentage of surgeons who do and who do not drain these areas.

From the Surgical Service, Beth David Hospital, New York, New York.

ANALYSIS OF DATA

It can be seen that 84 per cent of surgeons throughout the country routinely drain the gallbladder area. The duration of drainage varied from 2 to 6 days, with most men reporting removal of the drain on the fourth or fifth day. Sixty per cent of the surgeons stated that they removed the drain gradually, while 40 per cent removed the entire drain at one time.

As regards routine drainage of the duodenal stump following subtotal gastrectomy, except for surgeons in the East where 28.5 per cent use drainage, the large majority of the men close the abdomen tightly. In the country as a whole, the percentage of men who routinely drain the region of the stump is 17.7 per cent. Qualifications were made in many answers received, however, stating that if any doubt existed in the mind of the surgeon as to the insecurity of closure, drainage was instituted. Because of this fact, the overall percentage of duodenal stumps drained must be increased over that actually reported. The duration of drainage when instituted was longer in this group of patients than in the cholecystectomized group, varying from 3 to 10 days, with the seventh the mean day of removal. Again, the preferred method of removal was gradual (60 per cent).

TABLE I.—DATA ON USE OF DRAINS BY GEOGRAPHIC LOCATION

		East		Midwest		West		South		Total	
		No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Cholecystectomy	Drain	19	90	11	84	11	78.6	11	78.6	52	84
	No drain	2	10	2	16	3	21.4	3	21.4	10	16
Duodenal stump	Drain	6	28.5	2	16	2	14.2	1	7.1	11	17.7
	No drain	15	71.5	11	84	12	85.8	13	92.9	51	82.3
Localized intraperitoneal abscess	Drain	21	100	12	92.3	13	100	13	100	59	98
	No drain	0	0	1	7.7	0	0	0	0	1	2
Generalized peritonitis	Drain	4	20	2	16	0	0	4	30.7	10	16.4
	No drain	17	80	11	84	14	100	9	69.3	51	83.6
Exposed retroperitoneal tissue contaminated	Drain	9	45	10	58.8	11	91.7	7	53.9	37	59.7
	No drain	11	55	7	41.2	1	8.3	6	46.1	25	40.3
Not contaminated	Drain	3	15	5	29.4	2	15.4	0	0	10	16.1
	No drain	17	85	12	80.6	11	84.6	13	100		83.9

A localized intraperitoneal abscess was drained by 98 per cent of the surgeons who answered. This preponerance of opinion agrees well with what has been written in the older literature and with what are believed to be sound surgical principles. The drain is gradually removed by 90 per cent of the surgeons, and removal is completed by the seventh day.

Sentiment against drainage in generalized peritonitis was almost as strong as that for drainage of the localized abscess; 83.6 per cent of the surgeons stated that they did not drain generalized peritonitis, and many gave their reasons. Those given by Ravdin best express the general consensus and, therefore, are quoted, "We believe that generalized peritonitis is a diagnosis which can be made with assurance only at the autopsy table. If we find peritonitis at operation, we attempt to drain areas where we believe fluid collections might otherwise occur, and also drain the site of origin of the peritonitis. We do not believe that it is possible to drain the entire peritoneal cavity by any sort of drainage."

Fifty seven per cent of the replies favored drainage of exposed retroperitoneal tissue with contamination, while only 16.1 per cent favored it in uncontaminated cases. Again, the preferred method of removal was gradual (83 per cent).

Most surgeons expressed the opinion that uncontrollable intraperitoneal oozing was a problem that arose only rarely. From the 55 replies received in regard to this matter, 25 per cent of the surgeons used a Penrose drain, 24 per cent used gauze packing, 22 per cent used hemostatic agents, while 29 per cent did not use anything. Seventy per cent of the men stated that they removed the drains gradually.

Only 3 surgeons stated that their decision to drain was influenced by the type of suture material used. Although in most replies the type of suture used was not stated, in the majority of those in which it was given nonabsorbable material was the type indicated. Several men made note of the fact that when they used a drain with nonabsorbable suture material, the drain was brought out only through a stab wound and not through the incision.

Suction stump drainage was recommended frequently for drainage of localized fluid collections and when insecure duodenal stump closure was suspected.

DISCUSSION

The individual differences in replies do not indicate basic disagreement on principle, as all methods used have undoubtedly met with clinical success. We find that our own methods and observations coincide with the majority opinion in the survey. We believe that the indications for peritoneal drainage in intra-abdominal surgery are specific, that is in: (1) biliary tract surgery, to anticipate leakage of bile from the liver bed, aberrant ducts, and the cystic duct (the average amount of drainage of bile following an uncomplicated cholecystectomy is 150 cubic centimeters); (2) an abscess cavity with shaggy, necrotic, noncollapsing walls; (3) insecure closure of a hollow viscus with the anticipation of an intestinal fistula.

General peritonitis is an entity rarely if ever observed at the operating table. Localized peritonitis, if the peritoneum is intact, need not be drained in anticipation of abscess formation. In the absence of foreign material or necrosis, the peritoneum and the body defenses will overcome the infection. When the source of the infection or contamination remains, drainage should be instituted. When contamination has occurred as a result of the surgical procedure, either intraperitoneally or extraperitoneally, we are not inclined

to use drainage. Within the peritoneal cavity natural defensive powers will prevent the infection from spreading, and the use of antibiotics will contain and help to overcome infection in the extraperitoneal tissue. In cases such as this, the use of antibiotics prophylactically is indicated. Prophylactic chemotherapy should not be employed routinely in uncontaminated cases. Another important technical factor in the prevention of infection is the careful siphonage of all fluid exudates and blood from the recesses of the peritoneal cavity. These collections, especially when contaminated, are excellent culture media.

Although it has been our practice to use Penrose or cigarette latex drains, we believe that there is a convincing argument presented by those who use soft rubber tubes with continuous or intermittent suction since by and large drainage occurs by overflow rather than by capillary action and without mechanical removal of exudates the drain tends to become inspissated and to block rather than aid drainage.

Drains should be removed when all danger of escape of additional noxious material is passed. For the biliary tract this is sometime between the fourth and fifth day. In routine cases we remove drains by the fifth day.

Duodenal stumps have been known to rupture anytime between the second and fourteenth day. It is our belief, then, that drainage, if it must be instituted, should not be terminated before the seventh to eighth day. When localized intraperitoneal abscesses are drained, the drainage should be continued until the exudate becomes serous. After 10 days a sinus tract will become well established, and by that time the drain may be removed even if the exudate is still purulent. It matters little if drains are removed gradually or completely at one time. However, if gradual removal is used, the chance of secondary contamination is greater, and careful asepsis should be observed at the time of removal.

When there is a fair measure of difference of opinion in response to the questionnaire, arising from clinics of equal distinction, we believe that the decision as to drainage has been made on a purely personal basis and that equally good results may be obtained by both methods.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IN RECENT years, many monographs on orthopedic subjects have been published, but few have equaled Charnley's book, *Compression Arthrodesis; Including Central Dislocation as a Principle in Hip Surgery*,[1] in ease of reading and in the scientific and lucid presentation of a clinical subject. His style is entertaining, yet a great deal of information is presented in a relatively compact space. The illustrative material is excellent.

The value of the compression factor in arthrodesis of the knee and ankle has been established. Charnley now extends this principle to arthrodesis of other joints as well, particularly that of the hip. Not only are the clinical features of compression arthrodesis considered, but histologic studies and theoretic considerations are discussed in detail.

This, in the opinion of the reviewer, is an important monograph, not only because of its content, but also because it is an excellent example of good medical writing, original thought, and a stimulating presentation. Those who are interested in the subject and who do not thoroughly acquaint themselves with this volume will be the poorer because of their failure to do so. ROBERT A. KNIGHT.

IN THE preface to the volume *Roentgen-Diagnostics*[2] Dr. Case announces with very justifiable pride the presentation of the third of the 4 volumes of this encyclopedic text.

The present volume of approximately 1,100 pages is roughly divided into two parts. The first accounting for two-thirds of the text is devoted to the respiratory system and the last one-third to the heart and great vessels.

The various methods of examination of the thoracic contents are fully described and well illustrated. For example in the section on bronchography the use of water-soluble viscous contrast substances is outlined and discussed in a step by step manner. The problems confronting cardiac catheterization are likewise discussed and illustrated.

There are 3 chapters which deserve special mention. First, a chapter on roentgen follow-up after thoracic surgery by A. Brunner is very helpful in view of the recent rapid advances in thoracic surgery; second, a chapter on the differential diagnosis of diseases of the lungs, pleura, mediastinum, and diaphragm by U. Cocchi summarizes in tables and charts the roentgen findings which were discussed and illustrated in the first two-thirds of the book; and third, a chapter on the differential diagnosis of the heart and blood vessels by U. Cocchi. This last chapter is largely concerned with the most important congenital heart lesions.

As in the previous volumes the illustrations are most numerous, well chosen, and excellently reproduced. Also as in previous volumes the reproduced roentgenogram is in the fluoroscopic image.

The original generous bibliography carried in the German text at the end of each chapter has been supplemented in the American edition to include more material of English and American origin.

This particular volume carries its own index.

The tremendous amount of time, patience, and energy required of the editor of this American edition belies his emeritus status. Again we salute Dr. Case for this achievement.

This volume is highly recommended to the medical profession—the radiologist, the internist, and the thoracic surgeon. R. BURNS LEWIS.

THE fourth edition of *Die Kreuzschmerzen der Frau*[3] which is the book by Professor Martius on low back pain in women has been published. The arrangement of material and clarity of exposition is better than it was in the third edition. There is also a great improvement in the quality of the paper, type, and illustrations.

The author writes from wide experience, and as indicated from the bibliography has made a thorough review of the literature concerning low back pain. The need to consider the patient as a whole rather than from the specialist's narrow point of view is emphasized. At the same time the author considers it important to investigate all local conditions which may cause symptoms rather than to base the diagnosis on some vague constitutional disturbance. Consideration is given to psychic factors in

[1] COMPRESSION ARTHRODESIS; INCLUDING CENTRAL DISLOCATION AS A PRINCIPLE IN HIP SURGERY. By John Charnley, F.R.C.S., with chapters on Mechanics by Prof. J. A. L. Matheson, and Histological Observations by Prof. S. L. Baker. $8.50. 264 pages, 208 illustrations. Edinburgh & London: E. & S. Livingstone Ltd., 1953. Baltimore: The Williams & Wilkins Co., 1953.

[2] ROENTGEN-DIAGNOSTICS. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. 1st American ed., based on 5th German ed. Arranged and edited by James T. Case, M.D., D.M.R.E. (Camb.) Vol. 3. 3115 pages 3761 illustrations. $45.00. New York: Grune & Stratton, 1953.

[3] DIE KREUZSCHMERZEN DER FRAU; IHRE DEUTUNG UND BEHANDLUNG; GYNAKOLOGISCHE ORTHOPADIE. 4th rev. ed. By Prof. Dr. Heinrich Martius. 166 pages, 73 illustrations. DM 19.50. Stuttgart: Georg Thieme, 1953.

low back pain. These were particularly noticeable during the postwar period when a very common syndrome was low back pain associated with amenorrhea.

The nerve supply of the pelvic organs and the physiology of pain as it occurs in diseases of the pelvis are discussed. The author shows how mechanical disturbances in the pelvic organs can cause a reflex pain in the lumbosacral area and also discusses retroversion of the uterus, endometriosis, parametritis, and dysmenorrheas in general. The pelvic tumors as a causative factor in low back pain are mentioned.

In the second section of the book there is a discussion of body mechanics in women. The importance of the pendulous abdomen, visceroptosis, and pregnancy as factors in low back pain are emphasized.

Also shown is the relationship of pes valgo planus and high arches to statics of the back and low back pain. He recognizes back strain and speaks of static insufficiency as a common cause of low back pain.

It was found that two-thirds of the cases of backache in women are due to static decompensation and one-third to organic changes. Under those due to organic changes he includes scoliosis, spondylolisthesis, and displaced, ruptured nucleus pulposa. Finally, a differential diagnosis of low back pain is given.

This is an excellent treatise on low back pain in women. A good evaluation of the etiology, including gynecologic, anatomic, and functional factors, is presented. EMIL D. W. HAUSER.

THE 370 page monograph *A Handbook of Operative Surgery*[1] is designed and written to supply information concerning surgical procedures to those trained surgeons who have had little experience in this particular field. In this sense it is also a guide for the surgical resident. Although concerned chiefly with surgical operations which are described well the author has included a large amount of material on the diagnosis, preparation for operation, and the postoperative care.

The text is divided into four sections: the liver, the extrahepatic biliary system, the pancreas, and the spleen. Almost 40 per cent of the text is involved with the extrahepatic biliary system. The arrangement of the text is good. After sections outlining the condition under discussion from the standpoint of pathogenesis and diagnosis, all the standard operative procedures are described. The operative procedures are described in the text of the page facing well executed line drawings. The author's choice of operative procedures for illustration and description is sound and fairly represents current opinion in this country. Procedures which are controversial are pointed out.

This monograph was not designed as a reference work and consequently no references are included. In this field contributions have been made by so many workers that it would be difficult to give proper credit to them in such a text. An adequate index is included.

The author is to be congratulated on the nice arrangement of the text, the excellence of the line drawings made by Miss Jessie W. Phillips, and finally for a concise easily read monograph. The book will be found of most value by the surgical resident and those who though trained have had limited experience in these fields. THOMAS C. DOUGLASS.

THE authors of *Anatomy and Surgery of Hernia*[2] contend that too many surgeons perform hernia operations by rote without analyzing the relevance of the operative technique to the anatomic problem involved.

This very excellent text of 374 pages begins with a short historical review. The second chapter is devoted to a discussion of hernia in general. The common definition of hernia as a protrusion is inaccurate. Hernia is a defect or hole through which abdominal contents may protrude. The presence of a sac does not of itself constitute a hernia until some abdominal contents escape into the sac. The incidence, etiology, and clinical manifestations of hernia are described briefly. In discussing the treatment of hernia in general, the authors contend that the truss has no use except in the very rare instance in which spontaneous cure may still be expected, or wherein the patient's condition will not permit operation. The proper treatment of hernia is early surgical repair.

Chapter 3 is a very comprehensive description of the anatomy of the abdominal wall. To those readers who have seen Anson's *Atlas of Human Anatomy*, the illustrations will be familiar. Barry Anson and his associates have for many years been making painstaking and accurate studies of the fascial and muscular layers of the abdominal wall and have provided surgeons with a firm concept of these structures in both the normal muscular individual and the abnormally thin or the abnormally fat subject as well.

Chapters 4 through 11 are devoted to inguinal hernia. The anatomic structures involved in the etiology and pathology are described and illustrated. The young surgeon who finds it sometimes difficult to differentiate between indirect and direct inguinal hernia will be pleased to read that one with Doctor Zimmerman's wide clinical experience frequently cannot accurately distinguish between the two varieties before the canal is exposed at operation. In discussing the treatment of inguinal hernia, the authors condemn the injection treatment as being of limited scope, dangerous, and followed by a high percentage of failures.

Uncomplicated hernias in infants may close spontaneously with the aid of a truss during the

[1] A HANDBOOK OF OPERATIVE SURGERY. SURGERY OF THE BILIARY TRACT, PANCREAS, AND SPLEEN. By Charles B. Puestow, M.D., Ph.D. (Surg.). 370 pages, 72 illustrations. $9.00. Chicago: The Year Book Publishers, Inc., 1953.

[2] ANATOMY AND SURGERY OF HERNIA. By Leo M. Zimmerman M.D., and Barry J. Anson, Ph.D., (Med. Sc.). 374 pages, 204 illustrations. $10.00. Baltimore: The Williams & Wilkins Co., 1953.

first 6 months of life. Consequently, the authors prefer to delay operation until the age of 6 months. Surgical repair in infants is accomplished by simple excision of the sac and, where necessary, narrowing of the internal ring by single suture in the transversalis fascia.

The surgical treatment of inguinal hernia in adults is prefaced by an intelligent and logical criticism of many current misconceptions. In the reviewer's opinion, these pages are perhaps the most valuable and informative pages in the book. Logical repair of indirect hernia consists of removal of the preformed congenital sac and narrowing of the dilated internal ring to its original dimensions. Additional plications or transplantations are both unnecessary and harmful.

In the repair of direct inguinal hernia, the defect in the fascial floor of the inguinal canal must be repaired and supported by some type of plastic reinforcement. The authors accomplish this by repairing the defect in the transversalis fascia and reinforcing this with a flap from the lateral portion of the divided external oblique aponeurosis. This flap is sutured beneath the cord to the transversalis fascia. Nonabsorbable sutures are preferred in all repairs.

Chapters 12 and 13 are devoted to the anatomy and repair of femoral hernia. Few surgeons realize the frequency of recurrence of femoral hernia and hence the need for an intelligent repair. While one of several procedures may be satisfactory, the author prefers the use of an inguinal approach, closing the femoral ring by suturing a flap of external oblique aponeurosis over the ring to Cooper's ligament.

Chapter 14 deals with umbilical hernia and chapter 15 with ventral hernia. The most important factor in the treatment of incisional hernias is prevention by careful closure of primary incisions. Extraperitoneal repair is preferred for incisional hernia.

Chapter 16, written by Ralph B. Bettman, is devoted to diaphragmatic hernia. The surgical approach, whether abdominal, thoracic, or combined, must be based on an evaluation of the individual patient's problems and of the associated conditions as well.

Chapters 17 and 18 are devoted to a discussion of internal and pelvic hernias, and the book is concluded by a short discussion of the medicolegal aspects of hernia.

This text, in the words of the author, was not intended to be an encyclopedia of hernial surgery, yet it approaches almost that. The printing is clear, large, and easily readable, and the illustrations are excellent.

In the opinion of the reviewer, every man who has occasion to repair a hernia would benefit from reading this volume. It will be especially enlightening to the surgeon who for years has repaired every inguinal hernia by the same technique.

EDWARD W. GIBBS.

IN THE preface of *The Management of Pain*[1] which is an unusually fine book by John J. Bonica, the author states, "The purpose of this book is to present within one volume a concise but complete discussion of the fundamental aspects of pain, the various diseases and disorders in which pain constitutes a major problem, and the methods employed in its management, with special emphasis on the use of analgesic block as an aid in the diagnosis, prognosis, and therapy." He has succeeded admirably in accomplishing his purpose. A vast amount of material dealing with subjects, many of which are controversial and obscure has been gathered together, analyzed logically, and presented with a clarity that is not often found in works of this sort.

The book is divided into three major parts. Part 1 is devoted primarily to a discussion of the fundamental aspects of pain. Part 2 contains a complete discussion of all the useful methods and techniques of managing pain. Although the primary emphasis is on analgesic block, chapters are included on the use of opiates and other analgesics, psychotherapeutic methods, physical therapeutic methods, orthopedic methods, roentgen therapy, and neurosurgical methods in the management of pain. Part 3 is devoted to a description of pain syndromes and specific disorders or diseases which can be managed by "analgesic block with or without aid of other methods." The tables in this portion of the book are of considerable practical value. The author has provided a table for each region of the body. In these tables are listed all the diseases causing pain in that particular region. An example of a body region table is "Pain in the Shoulder." A brief description of the pain associated with each disorder or disease is given together with the page number on which this disease or disorder is fully described.

The volume is well illustrated and each chapter is followed by many references for those who wish to consult original sources. The book is one which will be of considerable interest and value to anyone who has to manage patients suffering with pain.

JOHN W. HIRSHFELD.

VOLUME I of *Ratna Hirurgija*[2] consists of 610 printed pages and contains 274 illustrations on the subject of war surgery. The publication is under the supervision of an editorial board of ten men and these with sixteen coauthors are responsible for the sixteen chapters which comprise the volume.

The first chapter has to do with the history of the surgery of wounds. Brief data are given concerning the contributions of Hippocrates, Celsus, Galen, Theodorico Borgognoni, Guy de Chauliac, Giovanni di Vigo, Paracelsus, Paré, LeDran, Larrey,

[1]THE MANAGEMENT OF PAIN; WITH SPECIAL EMPHASIS ON THE USE OF ANALGESIC BLOCK IN DIAGNOSIS, PROGNOSIS, AND THERAPY. By John J. Bonica, M.D. 1533 pages, 785 illustrations. $20.00. Philadelphia: Lea & Febiger, 1953.

[2]RATNA HIRURGIJA. By B. Brecelj, D. Dimkovic, B. Gusic, I. Kralj, B. Lavric, G. Nikolis, K. Oberslik, I. Papo, A. Telebakovic, and A. Zupancic. Vol. 1. 610 pages, 274 illustrations. Beograd: Izdanje Sanitetske Uprave Jna, 1953.

Pirogov, and Esmarch. The discussion is carried to the present time by including the contributions made by Serbian and Slovak leaders during World Wars I and II.

In the second chapter sanitation, field organization, evacuation of the wounded, operating pavilions, and medical records are considered. The third chapter presents the mechanism and classification of wounds including those occasioned by projectiles, the crush syndrome, and blast injuries. Shock, infections, gangrene, tetanus, wound healing, chemotherapy, and blood transfusion are discussed.

Other chapters are concerned with the rehabilitation of the wounded (physiotherapy, kinesitherapy, psychotherapy), asepsis and antisepsis, anesthesia, the treatment of burns, burns and other lesions in atomic warfare, plastic surgery, wounds of the extremities, of the knee joint, the treatment of fractures, amputations, and finally surgery of the circulatory system. To each chapter is appended a useful bibliography.

The book is printed in attractive type upon a good grade of paper. The tables and diagrams are clear and significant. The pictures are well reproduced. In some instances, however, they would be more effective if enlarged. The text is to be recommended to anyone who is familiar with the language of Jugoslavia. L. MARGUERIETE PRIME.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

GLOBAL EPIDEMIOLOGY; A GEOGRAPHY OF DISEASE AND SANITATION. By James Stevens Simmons, B.S., M.D., Ph.D., Dr.P.H., Sc.D. (Hon.), Tom F. Whayne, A.B., M.D., M.P.H., Dr.P.H., Gaylord W. Anderson, A.B., M.D., Dr.P.H., and Harold Maclachlan Horack, B.S., M.D. Associate author, Ruth Alida Thomas, B.A., A.M., M.P.H., and collaborators. Vol. III—The Near and Middle East. 357 pages, illustrated. $12.00. Philadelphia, London, Montreal: J. B. Lippincott Co., 1954.

MAMMALIAN GERM CELLS. A Ciba Foundation Symposium. Editor for the Ciba Foundation, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. Assisted by Margaret P. Cameron and Jessie S. Freeman. 302 pages, 54 illustrations. $6.75. Boston: Little, Brown & Co., 1953.

DISORDERS OF THE BLOOD; DIAGNOSIS: PATHOLOGY: TREATMENT: TECHNIQUE. By Sir Lionel E. H. Whitby, C.V.O., M.C., M.A., M.D. (Cantab.), F.R.C.P. (Lond.), D.P.H., and C. J. C. Britton, M.D. (New Zealand), D.P.H. 7th ed. 856 pages, with 20 plates and 106 text-figures. $9.50. New York: Grune & Stratton, Inc., 1953.

DIZZINESS; AN EVALUATION AND CLASSIFICATION. By David Downs DeWeese, M.D. 80 pages, 2 illustrations. $2.75. Springfield, Ill.: Charles C Thomas, 1954.

PELVIC RELAXATIONS AND HERNIATIONS. By James M. Wilson, M.D. 64 pages, 35 illustrations. $2.75. Springfield, Ill.: Charles C Thomas, 1954.

PRIMER RELATO OFICIAL: PERICARDITIS CONSTRICTIVA Y SU TRATAMIENTO QUIRURGICO. By Dres. Felix de Amesti Z. and Edgardo Collao C. Presented at the 9th Inter-American Congress and the 27th Chilean Congress. 114 pages, 22 illustrations. 1953.

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